

Comparison of once daily dose of 0.3% nepafenac alone and three times dose of 0.1% nepafenac alone in pain and inflammation control after phacoemulsification

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Purpose: To compare the efficacy of a once-daily dose of 0.3% nepafenac and three times daily dose of 0.1% nepafenac in controlling pain and inflammation following phacoemulsification. **Methods:** In this prospective randomized control single-blind study, patients who underwent uneventful phacoemulsification were divided into two groups. Group A received 0.1% nepafenac eye drops three times/day for 4 weeks and group B received 0.3% nepafenac eye drops once daily for 4 weeks following phacoemulsification. All the patients received moxifloxacin 0.5% eye drops four times/day for 2 weeks. None of the patients in any group received any form of corticosteroids. **Results:** The mean age of the patients in group A was 63.55 ± 8.5 years, while in group B, it was 60.05 ± 7.76 years. There was no significant result in the preoperative baseline demographics and intraoperative parameters between both the groups. The results were statistically insignificant in terms of inflammatory markers between both groups on day 1. But, on day 7, group B showed better results in terms of lid edema, conjunctival congestion, and anterior chamber cells. The patients in group B also perceived significantly less pain on day 1 ($P = 0.02$) and day 7 ($P < 0.001$). The central macular thickness was also significantly lower in group B at day 30 ($P < .001$) and day 90 ($P < .001$), respectively. **Conclusion:** Once-daily dose of higher concentrated nepafenac (0.3%) is equally effective and shows better results than 0.1% nepafenac for pain and inflammation control.

Key words: Inflammation, macular thickness, nepafenac, phacoemulsification, prednisolone

A cataract is the main cause of reversible blindness in the elderly population worldwide.^[1] Phacoemulsification is the most common elective ocular surgical procedure. The recent improvements in the surgical techniques, instruments, ophthalmic viscosurgical devices (OVD), and intraocular lens (IOL) have significantly reduced the complication rates in phacoemulsification, and have increased the patients' expectations of successful final outcomes.^[2] Anterior segment inflammation can be seen as an early postoperative complication following phacoemulsification. The intraocular surgery triggers an inflammatory response mediated by the cyclooxygenase (COX) enzymes and consequent release of other inflammatory mediators, mainly the prostaglandins. The prostaglandins cause a breakdown of the blood–aqueous barrier and increase the vascular permeability and accumulation of inflammatory cells and proteins in the anterior chamber.^[3] If left untreated for a longer duration, this inflammatory surge can cause pseudophakic cystoid macular edema (CME), posterior synechiae, and high intraocular pressure (IOP). Currently, steroids and non-steroidal anti-inflammatory drugs (NSAIDs) are used to control intraocular inflammation following phacoemulsification.^[4] Corticosteroids are usually

the preferred agents for inflammation control but they are associated with a few side effects like high IOP, late wound healing, proneness to infection, etc.^[5] NSAIDs are strong inhibitors of COX enzymes and prostaglandin production.^[6] The safety and effectiveness of topical NSAIDs in controlling intraocular inflammation and pain are well recognized, and the comparative advantages and risks of topical NSAIDs versus topical steroids in postoperative inflammation have been documented in the literature.^[4,7-9]

Nepafenac ophthalmic suspension 0.1% (Nevanac, Alcon laboratories, Inc) is a topical NSAID which is used to treat intraocular inflammation and reduce pain following phacoemulsification.^[10] In comparison to other topical NSAIDs, nepafenac is a prodrug that quickly infiltrates into the cornea and it deaminates into an active metabolite called amfenac by intraocular hydrolases within the vascularized tissues like the iris, ciliary body, retina, and choroid. Both nepafenac and amfenac are strong COX enzyme inhibitors.^[11] Due to

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the properties of greater corneal permeability, tissue-specific activation, longer duration of action, and sustained inhibition of prostaglandin release, nepafenac is regarded as a superior NSAID in comparison to the other topical NSAIDs.^[3,12] Furthermore, it has also shown effectiveness in reducing postoperative CME.^[13]

The US Food and Drug Administration (FDA) recently approved a new formulation of 0.3% nepafenac ophthalmic suspension (Ilevro, Alcon Laboratories Inc) to treat ocular inflammation and pain following phacoemulsification.^[14] The 0.3% nepafenac formulation has a greater concentration of active metabolite, reduced particle size for better absorption, and a guar as a retention agent which enhances the bioavailability in comparison to 0.1% nepafenac formulation.^[14] In this study, we compared the effectiveness of topical 0.1% nepafenac versus topical 0.3% nepafenac to control the postoperative anterior segment inflammation and pain following phacoemulsification.

Methods

This randomized, single-blind, single-center, interventional study was conducted after approval from the institutional review board (IEC/CPEH/19-01-11) and it adhered to the tenets of the Declaration of Helsinki. The study was conducted in a tertiary eye care center of northeast India from January 2019 to December 2019. All the participants were explained about the study and written informed consents were collected from them. The ethical approval from the institute ethics committee has been obtained. The date of approval= 07-01-2019.

Inclusion criteria

Patients aged more than 50 years with immature senile cataracts who had undergone uncomplicated phacoemulsification surgery with IOL implantation were enrolled in this study.

Exclusion criteria

- History of past intraocular surgery
- Patients with ocular comorbidities such as corneal opacity, glaucoma, pseudoexfoliation syndrome, uveitis, lens subluxation, poor mydriasis, retinal pathology, and macular diseases were excluded from the study.
- Intraoperative complications like posterior capsular rent, zonular dehiscence, vitreous loss, posterior dislocation of whole nucleus or fragments, iris damage, etc.
- Patients who used systemic or topical steroids 2 weeks before the surgery, received steroid injection by any route 3 months before the surgery, and received systemic and topical NSAIDs 7 days before the surgery were excluded from the study
- Patients who lost to follow-up
- Systemic diseases like diabetes mellitus, uncontrolled hypertension, known allergy to nepafenac.

Sample size calculation

The sample size was calculated using Open Epi software version 3.01 (<http://www.openepi.com>). Considering the confidence interval (two-sided) of 95% and power as 80%, the estimated sample size was 140 in each group based on the mean difference of the anterior chamber (AC) cell score between the two groups (mean AC cells score difference between the two groups, 0.07) in a similar study by Sarkar *et al.*^[4]

Preoperative evaluation

A complete ocular examination including uncorrected visual acuity (UCVA), best-corrected visual acuity (BCVA), slit-lamp examination for grading of the cataract and assessment of the anterior segment, IOP measurement with Goldman applanation tonometer, central corneal thickness (CCT), and dilated fundus examination was performed for each patient. The grading of the cataract was done according to the lens opacities classification system III (LOCS III).^[15] The optical coherence tomography (OCT) was done before the surgery in each patient preoperatively to evaluate the central macular thickness (CMT).

Group randomization

All the recruited patients were categorized into two groups (A and B) using the computerized randomization method. Nepafenac 0.1% (Nevanac; Alcon Laboratories, Inc) eye drops were prescribed in group A at a dose of three times/day for 4 weeks, while 0.3% nepafenac (Ilevro, Alcon Laboratories, Inc) eye drops were prescribed once daily for 4 weeks in group B. The nepafenac eye drops in both groups were started immediately after the surgery. The patients did not receive any topical or systemic NSAIDs in the preoperative period. Moxifloxacin 0.5% eye drops (Vigamox, Alcon Laboratories, Inc) four times/day were started 2 days prior to surgery till 2 weeks postoperatively in both the groups. None of the patients in both groups received any form of corticosteroids during the entire postoperative period. The operating surgeon, resident doctor, and optometrist who were performing the preoperative, intraoperative, and postoperative evaluations were blinded about the study groups.

Operative procedure

A single experienced surgeon (NB) performed all the cases under topical anesthesia (proparacaine 0.5% eye drops, Senses pharmaceuticals, India). A 2.2 mm temporal limbal incision was created, a 5–5.5 mm capsulorhexis was performed with a 30 G bent cystitome and a cortical cleavage hydrodissection was done in each case. The nucleus was managed with torsional phacoemulsification with active fluidics (Centurion Vision System, Alcon Laboratories, Inc) using a standard direct chop technique.^[16] Balanced salt solution (BSS) was used as an irrigation agent. A foldable, single-piece, hydrophobic, acrylic IOL was injected in the capsular bag;^[17] 0.5 mL of preservative-free moxifloxacin (0.5%; Vigamox, Alcon Laboratories, Inc) was injected in the AC at the end of the surgery. No eye patch was applied at the end of the surgery.

Postoperative follow-up

Postoperative follow-up was done for all the patients on days 1, 7, 30, and 90, respectively. UCVA, BCVA, IOP measurement, slit-lamp examination to grade the AC reactions, and dilated fundus examination were done at each visit. Each patient was examined by the same senior resident doctor on each visit to document the signs of inflammation such as lid edema, conjunctival congestion, corneal edema, AC cells, and flare. Posterior segment examination was done to assess any signs of vitritis and macular edema. Intraocular inflammation was graded according to the standardization of uveitis (SUN) nomenclature working group classification.^[18]

Table 1: Demographic and preoperative parameters

Parameters	0.1% Nepafenac	0.3% Nepafenac	P
Total no. of patients	137	137	
Age (Years)	63.55±8.5	60.05±7.76	0.68
Sex			
Male	76 (55.8%)	72 (52.9%)	
Female	61 (44.2%)	65 (57.1%)	
LOCS III			
I	2 (1.46%)	1 (0.73%)	
II	81 (59.12%)	73 (53.28%)	
III	41 (29.93%)	53 (38.69%)	
IV	13 (9.49%)	10 (7.3%)	
Mean±SD			
Axial length (AL)	22.94±0.9	23.15±2.16	0.31
K mean (D)	44.53±0.9	45.71±1	0.11
IOP (mmHg)	13.79±2.16	13.82±2.83	0.9
CCT (microns)	530±12	517±13	0.2
BCVA (logMAR)	0.72±0.33	0.76±0.31	0.34
CMT (microns)	257.9±17.8	261.7±16.2	0.09
ECD (cells/mm ²)	2538±184	2516±197	0.33

Unpaired t-test. IOP=Intraocular pressure, CCT=Central corneal thickness, BCVA=Best-corrected visual acuity, CMT=Central corneal thickness, ECD=Endothelial cell density

Table 2: Intraoperative parameters

Parameter	0.1% Nepafenac	0.3% Nepafenac	P
Surgical time (min)	13.32±2.1	13.38±2.1	0.8
CDE	9.06±2.28	10.34±3.1	0.21
Ultrasound time (sec)	43.34±12.8	44.14±16.3	0.64
Aspiration time (s)	172.39±54.1	174.26±55.9	0.78
BSS volume used (mL)	113.2±27.03	122.13±31.22	0.75

Unpaired t-test

Grading

Lid edema, conjunctival congestion, and corneal edema were graded based on a similar study published by the same authors.^[4] Lid edema grade: mild swelling with visible lid creases was grade 1, moderate swelling with minimally affected lid creases was grade 2, severe swelling with not able to open eyelids actively was grade 3, and extreme swelling with not able to open eyelids actively was grade 4. According to the SUN classification, the AC cells (in 1 mm² slit illuminating beam in AC) were graded as grade 0 for less than 1 cells, grade 0.50 for 1–5 cells, grade 1 for 6–15 cells, grade 2 for 16–25 cells, grade 3 for 26–50 cells, and grade 4 for > 50 cells. AC flare (slit-lamp, 1 mm² slit beam) was graded as grade 0: no flare, grade 1: faint, grade 2: moderate (anterior chamber structures clearly visible), grade 3: marked (anterior chamber structure details hazily seen), and grade 4: intense reaction (fibrinous membrane/plastic aqueous). Conjunctival congestion was graded as grade 0 for no hyperemia, grade 1 for sectoral engorgement of vessels, grade 2 for diffuse engorgement, and grade 3 for significant engorgement. Corneal edema (slit-lamp examination) was graded as grade 0: no stromal or epithelial edema, slight stromal edema as

grade 1, diffuse stromal edema as grade 2, diffuse stromal edema with microcystic edema of the epithelium as grade 3, and bullous keratopathy as grade 4.

Posterior segment evaluation with indirect ophthalmoscopy and 90 D lens was done at each visit. The OCT (Cirrus HD-OCT; Carl Zeiss Meditec) was performed at days 30 and 90 to look for CMT and evidence of CME. Each patient was provided a visual analog scale (VAS) at every visit to categorize their ocular pain. The scale is comprised of a 10-point scoring system, where 0 point means no pain and 10 points means the worst pain ever acknowledged by the patient. The patients were asked to mark the points to indicate the severity of the ocular pain that the patients experienced at each visit.

Data were analyzed using IBM SPSS Statistics ver. 26 (IBM Corp., USA). Group comparisons were performed with the Mann–Whitney test. Visual acuity was converted to logMAR units for analysis purposes. Chi-square test, unpaired t-test, and correlations were performed whenever needed. A P value less than 0.05 was considered significant.

Results

A total of 280 patients were recruited in the study, but six patients lost to follow-up after the first visit. So, they were not included in the final analysis. Group A had a total of 137 patients: 76 (55.8%) males and 61 (44.2%) females. Similarly, group B also had 137 patients: 72 (52.9%) males and 65 (57.1%) females. The mean age of the patients in group A was 63.55 ± 8.5 years, while in group B, it was 60.05 ± 7.76 years (P = 0.68). The demographic profile and the intraoperative parameters in both groups [Table 1]. There was no difference between the surgical parameters between the groups [Table 2].

The mean BCVA in group A improved from 0.72 ± 0.33 logMar in the preoperative period to 0.1 +/- 0.09 logMar in 1 month postoperatively (P < .001). Similarly, the mean BCVA in group B improved from 0.76 ± 0.31 logMar in the preoperative period to 0.1 ± 0.08 logMar in 1 month postoperatively (P < .001). There was no statistically significant difference in terms of BCVA at the 1 month postoperative period between both the groups (P = 0.02).

Parameters of postoperative inflammation

Postoperative inflammatory markers such as lid edema, conjunctival hyperemia, corneal edema, AC cells, AC flare, and IOP in both the groups on postoperative days 1, 7, and 30 are shown in Table 3.

The mean scores of lid edema in group A were 1.25, 0.76, 0.00 on days 1, 7, 30, respectively, while in group B, they were 1.15, 0.47, 0.00, on days 1, 7, 30, respectively. The comparison of the mean scores of lid edema between the groups showed no statistical difference on day 1 (P = 0.46), but on day 7, the difference was statistically significant (P < 0.001). None of the patients in both the groups had lid edema on day 30.

The comparison of conjunctival congestion revealed no statistical difference between the groups on day 1 with a P value of 0.67. However, on day 7, there was a statistically significant difference in the mean scores between the groups (P = 0.01). On day 30, none of the patients in both groups had evidence of conjunctival congestion.

Table 3: Comparison between postoperative inflammatory markers

Parameter	DAY 1			DAY 7			DAY 30		
	0.1%	0.3%	P	0.1%	0.3%	P	0.1%	0.3%	P
Mean score of lid edema	1.25	1.15	Z=0.73, P=0.46	0.76	0.47	Z=3.53, P<0.001	0	0	
Mean score of Conjunctival hyperemia	0.83	0.8	Z=0.43, P=0.67	0.51	0.34	Z=2.51, P=0.01	0	0	
Mean score of Corneal edema	0.94	0.82	Z=1.14, P=0.25	0.52	0.39	Z=1.20, P=0.23	0	0	
Mean score of AC cells	1.02	0.98	Z=0.30, P=0.76	0.67	0.55	Z=2.32, P=0.02	0	0	
Mean score of AC flare	0.12	0.12	Z<0.001, P=1	0	0		0	0	
IOP (Mean±SD)	16.55±2.6	16.59±2.68	Z=0.22, P=0.82	15.52±2.43	15.55±2.52	Z=-0.22, P=0.83	15.18±2.38	15.21±2.76	Z=-0.23, P=0.83

Mann-Whitney U test

Similarly, while comparing both the groups in terms of corneal edema, there was no statistical difference in the mean scores on day 1 and day 7 with *P* values of 0.25 and 0.23, respectively. On day 30, none of the patients in either group had corneal edema.

The comparison of the mean scores of AC cells did not reveal any statistically significant difference on day 1 (*P* = 0.76), but on day 7, a significant difference (*P* = 0.02) was noted between the two groups. At day 30, there was no evidence of AC cell in any of the patients in both the groups.

There was no statistically significant difference in the mean scores of AC flare between both groups on day 1 (*P* = 1). No AC flare was noted in any patient in both groups on day 7 and day 30 of the postoperative visit.

The mean preoperative IOP in group A and group B was 13.79 ± 2.16 mmHg and 13.82 ± 2.83 mmHg, respectively. The comparison of the intraocular pressure (IOP) between the two groups did not exhibit any statistically significant difference on day 1 (*P* = 0.82), day 7 (*P* = 0.83), and day 30 (*P* = 0.83). There was a rise of intraocular pressure in both the groups in comparison to the preoperative IOP on day 1 (*P* < .001) and day 7 (*P* < .001), but the mean IOP during the entire postoperative period in both the groups was within the normal limit.

Table 4 shows the comparison of the pain scores between the two groups. There was a statistically significant difference between both the groups in terms of the mean pain scores (2.13 vs. 1.82 in groups A and B, respectively, *P* = 0.02) on postoperative day 1. On day 7 also, the mean pain score was significantly lower in group B (1.2 in group A vs. 0.55 in group B, *P* = <.001).

Central macular thickness

The comparison in the mean CMT between the groups showed a significant difference (281.29 ± 12.31 microns in group A vs. 266.05 ± 6.1 microns in group B, *P* < 0.001) on day 30 as well as on day 90 (276.25 ± 12.25 microns vs. 262.11 ± 6.34 microns in groups A and B, respectively, *P* < 0.001) [Tables 5 and 6].

Discussion

Phacoemulsification is the most commonly performed cataract surgical technique worldwide. Newer developments in surgical

Table 4: Comparison of the visual analog score (VAS)

Group	Day 1	P	Day 7	P	Day 30	P
0.1%	2.13	Z=2.28	1.2	Z=4.99	0	
0.3%	1.82	P=0.02	0.55	P<0.001	0	

Mann-Whitney U test

techniques and equipment have improved postoperative outcomes drastically. However, all cataract surgeries are invariably associated with some degree of postoperative inflammation. In addition, an exaggerated postoperative inflammation can be observed sometimes in conditions like diabetes mellitus, small pupil, uveitis, brown cataract, pseudoxfoliation, posterior capsular rupture, nucleus drop, etc.^[3,19] Untreated ocular inflammation can lead to raised IOP, CME, and posterior capsular opacification.^[4]

Steroids and NSAIDs are the two groups of drugs commonly used for the treatment of postoperative inflammation. However, steroid usage may be associated with side effects like delayed wound healing, increased risk of infection, and glaucoma.^[20] The use of NSAID eye drops can help to prevent these steroid-related side effects. NSAIDs are potent inhibitors of the COX enzymes, and thereby, inhibit prostaglandin production. The efficacy and safety of topical NSAIDs in treating ocular inflammation and pain are well established. Topical NSAIDs are also beneficial for the treatment of post-cataract surgery CME, CME in uveitis, CME in retinal vein occlusions, etc.^[10]

Nepafenac is a topical NSAID which rapidly permeates through the cornea and gains intraocular entry. It is transformed to the active molecule, amfenac, in the intraocular vascularized tissues. Amfenac is a strong inhibitor of COX-1 and COX-2 pathways that catalyze the formation of proinflammatory prostaglandins.^[9,21]

There are various prior studies which had reported the efficacy of topical NSAIDs in the control of postoperative intraocular inflammation. In a study by Sarkar *et al.*,^[4] topical 0.1% nepafenac alone was found to be more effective (*P* = 0.018) than topical 1% prednisolone acetate alone in ocular pain control after cataract surgery. Maxwell *et al.*^[22] showed in

Table 5: Final postoperative outcomes

Parameter	Day 30			Day 90		
	0.1%	0.3%	P	0.1%	0.3%	P
BCVA (log MAR)	0.1±0.09	0.08±0.08	Z=2.20, P=0.02	0.1±0.08	0.07±0.08	Z=2.30, P=0.02
CMT (microns)	281.29±12.31	266.05±6.1	Z=9.16, P<.001	276.25±12.25	262.11±6.34	Z=7.16, P<.001
ECD (cells/mm ²)	2284±188	2351±187	Z=0.97, P=0.13	2249±197	2333±190	Z=-0.87, P=0.39

Mann-Whitney U test. BCVA=Best-corrected visual acuity, CMT=Central corneal thickness, ECD=Endothelial cell density

Table 6: Comparison between both the groups with respect to macular thickness

Group	Preoperative	POD 30	P	Mean change (microns)	P
0.1%	257.9±17.8	281.29±12.31	t=9.63, P<0.001	17.29±12.33	Z=5.25,
0.3%	261.7±6.2	266.05±16.1	t=-0.62, P=0.43	4.35±8.46	P<.001

Paired t-test, Mann-Whitney U test

their study that four times/day (QID) dose of 0.1% nepafenac was more effective than once daily (OD) or two times/day (BD) dose of 0.1% nepafenac in controlling pain following cataract extraction. In another study by Naithani *et al.*,^[21] 0.1% nepafenac was found to be better than the placebo drops in the prevention of ocular pain following vitreoretinal surgery. In phase II placebo-controlled study by Jiro Numaga, 0.1% nepafenac showed better results than placebo drops in the treatment of ocular pain following cataract surgery.^[23]

The current study is only the second study to the best of our knowledge which compared the efficacy of 0.1% nepafenac alone with 0.3% nepafenac alone in controlling postoperative inflammation and pain. The results of our study suggest that once-daily dose of 0.3% nepafenac is superior to the three times daily dose of 0.1% nepafenac for the prevention of postoperative pain (day 1 and day 7 postoperatively) after cataract surgery; 0.3% nepafenac was also found to be more effective than 0.1% nepafenac in the treatment of postoperative inflammation as observed from the statistically significant difference in the mean scores of the AC cells between the groups on day 7 after surgery. However, there was no statistically significant difference between both the groups in terms of prevention of other inflammatory parameters such as lid edema, conjunctival congestion, cells and flare in the AC, corneal edema, and IOP on day 1 postoperatively. But, on postoperative day 7 (POD 7), 0.3% nepafenac was found to be more effective than 0.1% nepafenac in the treatment of lid edema and conjunctival congestion. Modi *et al.*^[14] also reported similar results in their phase 3 clinical trial; 0.3% nepafenac showed better results than 0.1% nepafenac in controlling the postoperative inflammation.

The mean pain severity score in the 0.3% nepafenac group was significantly lower than the 0.1% nepafenac group on POD 1 ($P = 0.02$) as well as on POD 7 ($P < .001$) in the current study. In the study by Modi *et al.*,^[14] nepafenac 0.3% once-daily dose was reported to be equivalent to nepafenac 0.1% three times the daily dose for the management of ocular pain following phacoemulsification.

The mean CMT was significantly lower in the 0.3% nepafenac group compared to the 0.1% nepafenac group (281.29 ± 12.31 microns vs. 266.05 ± 6.1 microns, $P < .001$) on POD 30 and POD 90 (276.25 ± 12.25 microns vs. 262.11 ± 6.34 microns, $P < .001$) in our study. In a study by Tzelikis *et al.*,^[24] 0.3% nepafenac

was found to be more effective ($P < .001$) than placebo eye drops in reducing CMT at 5 weeks postoperatively. Zaczek *et al.*^[25] in their study showed that nepafenac 0.1% was better than the placebo treatment on reducing macular thickness at 3 weeks ($P < .001$) and 6 weeks ($P = 0.022$) following cataract surgery. In a study by Miyake *et al.*,^[13] 0.1% nepafenac showed better results than fluorometholone in reducing CMT following phacoemulsification. A few other studies have also shown that topical 0.1% nepafenac is very effective in controlling pseudophakic macular edema.^[4,26] However, the current study is the first one to compare the efficacy of 0.1% nepafenac versus 0.3% nepafenac in preventing pseudophakic CME.

To summarize, the role of 0.1% nepafenac in controlling intraocular inflammation, pain, and CME following cataract extraction is well documented. Prior studies have already shown nepafenac 0.1% eye drops to be non-inferior to prednisolone eye drops in controlling inflammation following cataract surgery. In our study, we went a step further to compare the efficacy of the newer 0.3% nepafenac formulation with 0.1% nepafenac in controlling pain and inflammation following uncomplicated phacoemulsification. The results of the current study have shown that once-daily dose of 0.3% nepafenac is comparable to the usual three times daily dose of 0.1% nepafenac in controlling pain and inflammation after phacoemulsification.

Conclusion

To the best of our knowledge, our study represents the first prospective randomized study which compares the efficacy of 0.3% nepafenac once-daily dose alone versus 0.1% nepafenac three times daily dose alone in controlling the postoperative pain and inflammation after phacoemulsification with promising results.

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Conflicts of interest

There are no conflicts of interest.

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