Comparison between 0.1% Nepafenac and 1% Prednisolone Eye Drop in Postoperative Management Following Micro-incisional Cataract Surgery

Sandip Sarkar¹, Narayan Bardoloi¹, Amit Kumar Deb²

¹Cataract & Cornea Services, Chandraprabha Eye Hospital, Jorhat, India
²Department of Ophthalmology, Jawaharlal Institute of Postgraduate Medical Education and Research, Puducherry, India

**Purpose:** To compare the efficacy of 0.1% nepafenac and 1% prednisolone acetate eye drop in postoperative inflammation control in micro-incisional cataract surgery.

**Methods:** We conducted a prospective, randomized, comparative, single-blind study. All the patients underwent temporal 2.2-mm micro-incisional cataract surgery. They were randomized into two groups (group A and B). Group A received 0.1% nepafenac eye drops 4 times/day for 4 weeks and group B received 1% prednisolone acetate eye drops in tapering doses for 4 weeks after surgery. Both the groups received moxifloxacin 0.5% eye drops 4 times/day for 2 weeks. Patients were examined on 1st, 7th, and 30th postoperative days and parameters of postoperative inflammation were evaluated and noted at each visit.

**Results:** A total of 200 patients were enrolled in the study. However, five patients lost to follow up, group A had 97 and group B had 98 patients respectively. Results were statistically insignificant in terms of the difference in lid edema, conjunctival congestion, corneal edema, anterior chamber cells and flare between the two groups with p-values >0.05 for each parameter at each visit. However, the difference in mean central macular thickness between the groups was significant (205.713 ± 17.14 vs. 220.984 ± 32.83 in group A and B, respectively, p ≤ 0.001) at 1 month. Also, the mean pain score was significantly lower (p = 0.018) in the nepafenac group at day 7 of surgery.

**Conclusions:** Nepafenac is equally effective and non-inferior to prednisolone acetate in suppression and prevention of inflammation in postoperative period.

**Key Words:** Cataract, Inflammation, Macular edema, Nepafenac, Prednisolone acetate

Phacoemulsification remains one of the most commonly performed elective surgical procedure worldwide [1]. The improved surgical methods and newer instruments have significantly decreased the surgical complications, and have been able to increase the expectation level of a successful visual outcome [2,3]. Anterior segment inflammation is regarded as one of the most commonly occurred complications following phacoemulsification. Intraocular inflammation breaks down the blood-aqueous barrier and
increases the production of inflammatory proteins and cells into the aqueous humour. Uncontrolled postoperative ocular inflammation for longer duration can lead to pseudophakic cystoid macular edema (CME), synechiae development, and elevated intraocular pressure (IOP). Recent advancements in surgical techniques and better quality of viscoelastic ensures a decrease in surgery-related physical trauma. This, in return, causes a reduction in the release and development of the chemical mediators of postoperative ocular inflammation [4]. Currently, steroids and non-steroidal anti-inflammatory drugs (NSAIDs) are the two sets of the drug which are available to control intraocular inflammation [4-6]. Corticosteroids have been the mostly commonly used anti-inflammatory agent following cataract surgery [7]; but it can cause few side effects such as raised IOP, inhibit wound healing, increased chances of infection etc. [8]. Topical corticosteroids currently available are dexamethasone, prednisolone acetate, fluorometholone, difluprednate, etc. On the other hand, the currently available topical NSAIDs for postoperative ocular inflammation are bromfenac, diclofenac, ketorolac, and nepafenac [9]. Nepafenac is a prodrug that deaminates into an active metabolite, amfenac by intraocular hydrolysis within iris, ciliary body, retina, choroid. It also shows superior corneal permeability, thereby, achieving higher intraocular drug concentration compared to other NSAIDs. Most importantly, nepafenac causes sustained inhibition of prostaglandin synthesis in comparison to other NSAIDs. The better absorption, tissue specific activation, and prolonged period of action of nepafenac make it superior than other NSAIDs for inflammation control following micro-incisional cataract surgery (MICS) [10]. In this prospective comparative study, we compared the effectiveness of topical NSAID drug nepafenac (0.1%) alone with topical corticosteroid drug prednisolone acetate (1%) to control the intraocular inflammation following MICS.

**Materials and Methods**

We did a prospective, randomized, single-blind, single-center comparative clinical interventional study in a tertiary eye care center in North-East India. Participants were registered in the study based on the inclusion and exclusion criteria from the patients with senile cataract requiring phacoemulsification surgery. The study approval was obtained from the institutional ethics committee (IEC/CPEH/19-01-05) and it adhered the tenets of the Declaration of Helsinki. Written informed consent was obtained from all the participants after explaining the whole study to them.

**Inclusion criteria**

Patients with age >50 years and immature senile cataracts requiring phacoemulsification were recruited in the study.

**Exclusion criteria**

Patients with presenile cataract, glaucoma, uveitis, complicated cataract, subluxated cataract, traumatic cataract, posterior segment pathology were excluded. Patients with ocular pathology like corneal opacity, angle closure glaucoma, pseudo exfoliation syndrome, poor mydriasis were also excluded. Complications during phacoemulsification like posterior capsular rupture, zonulodalysis, vitreous loss, nucleus drop, iris trauma etc. were also excluded. Patients who have taken any form of steroids within 2 weeks of surgery, undergone intraocular or periocular injection of steroids within 3 months of surgery, taken either systemic or topical NSAIDs within 7 days of surgery, diabetic melitus, uncontrolled hypertension and patients with ocular allergy to nepafenac were also excluded from the study.

**Sample size calculation**

The sample size for our study was calculated in OpenEpi ver. 3.01 (http://www.openepi.com). Considering confidence interval (2-sided) of 95% and power as 80%, the estimated sample size was 99 for each group based on the difference in the mean anterior chamber (AC) cell score between the two groups (group 1 had mean AC cell score 1.10 and group 2 had 1.20) in a similar study by Nagpal et al. [6].

**Preoperative evaluation**

All the patients underwent comprehensive ophthalmic evaluation including uncorrected visual acuity (UCVA), best-corrected visual acuity (BCVA), slit-lamp examination to grade the cataract and assess the anterior segment,
IOP with Goldmann applanation tonometer, and fundus examination using indirect ophthalmology with 20 D lens. Lens opacities classification system III (LOCS III) [11] was used to grade the cataract.

**Group allocation**

Enrolled patients were categorized into two groups using simple randomization technique. Group A received nepafenac 0.1% (Nevanac; Alcon Laboratories, Fort Worth, TX, USA) eye drops 4 times/day over 4 weeks. Group B received prednisolone acetate 1% (Predforte; Allergan, Bangalore, India) eye drop 4 times/day in tapering doses for 4 weeks. Eye drops were started from the day of surgery. Both groups received additional Moxifloxacin 0.5% eye drops (Vigamox, Alcon Laboratories) 4 times/day for 2 weeks. Systemic NSAIDs were not provided to any of the patients in both groups. Topical NSAIDs were started only after 4 hours of the surgery, none of the patients received NSAIDs preoperatively. Postoperative management of the patients in both the groups has been delineated in

![Fig. 1. Showing the management protocol of both the groups following micro-incisional cataract surgery (MICS). FU = follow-up; QID = four times a day; BCVA = best-corrected visual acuity; IOP = intraocular pressure; VAS = visual analog scale; OCT = optical coherence tomography.](image)

**Surgical technique**

A single experienced surgeon (NB) performed all the surgeries under topical anaesthesia (proparacaine 0.5% eye drops). Povidone-iodine (10%) solution was used to disinfect the skin around the operative site, and a 5%-solution was applied to the lower conjunctival sac 3 minutes prior to the surgery. Two, 1-mm side port incisions were made at 2 and 8 o’clock positions with microvitreoretinal blade. A triplanar temporal limbal 2.2-mm incision was created with the help of a dual bevel keratome (Alcon Laboratories) in every case. A 5- to 5.5-mm capsulorhexis was performed using a 30-gauze cystitome. All the patients undergone torsional phacoemulsification in an active fluidic system (Centurion Vision System, Alcon Laboratories) with a balanced tip. Balanced salt solution (Alcon Laboratories) was used as an irrigation solution in every case. The nucleus was divided with chop in situ [12] technique in majority of the cases, whereas, in cases of hard cataract a central crater was made and a stop and chop technique [13] were used to facilitate the division. After nuclear emulsification, bimanual irrigation and aspiration was used to aspirate the cortical matter. A foldable, single piece, hydrophobic, acrylic intraocular lens was injected in the capsular bag with hydro implantation technique [14]. Intracameral preservative-free moxifloxacin (0.5%; Vigamox, Alcon Laboratories) was injected in all cases. The main incision and sideport incisions were closed using stromal hydration.

**Postoperative follow-up**

All the patients were examined on day 1, 7, and 30, postoperatively. Uncorrected visual acuity, BCVA and IOP measurements were done at every visit. Complete ophthalmic evaluation including slit lamp examination was done to look for lid edema, conjunctival hyperemia, corneal edema, cells and flare in the AC each visit by the same resident. Posterior segment examination was done by the same resident to assess any signs of inflammation in the vitreous. Anterior segment inflammation was graded using the standardization of uveitis nomenclature working group classification [15].
Grading

The cells in the AC was graded using a 1mm thin slit beam of a slit-lamp as follows: grade 0 was no cells, grade 0.50 was 1–5 cells, grade 1 was 6–15 cells, grade 2 was 16–25 cells, grade 3 was 26–50 cells, and grade 4 was more than 50 cells.

Flare in the AC (slit-lamp examination, using a 1-mm slit beam) was graded as follows: grade 0 was none, grade 1 was faint, grade 2 was moderate (iris/lens details clear), grade 3 was marked (iris/lens details hazy), and grade 4 was intense (fibrin/plastic aqueous).

Lid edema was graded as follows: minimal swelling with lid creases visible was grade 1, moderate swelling with skin creases affected was grade 2, marked swelling when eyelids could be opened actively was grade 3, and extreme swelling when eyelids could not be opened actively was grade 4. Conjunctival hyperemia 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 follows: no stromal or epithelial edema was grade 0, 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 [6].

Fundus examination was done at each visit. However, on day 30, special attention was given to detect any evidence of CME. Optical coherence tomography (Cirrus HD-OCT; Carl Zeiss Meditec AG, Dublin, CA, USA) was done at day 30 to determine the central macular thickness (CMT) and look for any evidence of CME.

A visual analog scale (VAS) was given to all the patients on each day during follow up visits to grade the ocular pain. The VAS consisted of a 10-cm line, with 0 on one end meaning no pain and 10 on the other meaning the worst pain ever experienced. The patients were told to mark on this line to indicate the severity of pain he or she felt during the follow-up period. The VAS was filled up by the patients on each follow-up.

Data were analyzed using IBM SPSS Statistics ver. 20 (IBM Corp., Armonk, NY, USA). A frequency distribution with its percentage and descriptive statistics with mean and standard deviation were calculated. 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 200 participants criteria were included in the study, among them, five patients did not complete all mandatory follow up visits and were, therefore, excluded during analysis. All the five patients lost to follow up after the first visit on postoperative day 1. Data from 195 participants were available for analysis. Group A had 97 participants of which 64 (66%) were males and 33 (34%) were females. Patients in group A had a mean age of 67.92 ± 7.61 years. Group B had 98 participants of which 58 (59.2%) were males and 40 (40.2%) females. Patients in group B had a mean age of 69.42 ± 4.84 years. Both groups were, therefore, matched in terms of demographic features. Baseline characteristics of the patients are mentioned in Table 1.

BCVA and IOP

Postoperative visual acuity outcomes in both groups are compared in Table 2. The mean logMAR postoperative BCVA in both the groups at day 1 (p = 0.92), day 7 (p = 0.37) and day 30 (p = 0.56) after surgery was statistically insignificant. Similarly, IOP differences between both the groups also showed no statistical significance on day 1 (p = 0.31), day 7 (p = 0.20), and day 30 (p = 0.15).

Parameters of postoperative inflammation

Postoperative parameters of inflammation including lid edema, corneal edema, conjunctival hyperemia, AC cells and AC flare in both the groups on postoperative day 1, 7, and 30 are compared in Table 3.

Comparison of the mean score of AC cells between both the groups showed no difference on day 1 (p = 0.62) and day 7 (p = 0.69). No AC cells were noted in both the groups at day 30 of follow-up.

Comparison of the mean score of AC flare between both the groups showed no difference on day 1 (p = 0.42). There was no AC flare in both the groups at day 7 and 30 of follow-up.

Comparison of lid edema between the two groups in the postoperative period showed no statistical difference on day 1 (p = 0.68), day 7 (p = 0.84). At day 30, no patient in either group had any evidence of lid edema.

Comparison of conjunctival hyperemia in both the
### Table 1. Baseline characteristics of both the groups

| Parameter                              | Group | Measurement | Statistics | p-value |
|----------------------------------------|-------|-------------|------------|---------|
| Mean age (yr)                          | A     | 67.92 ± 7.61| t = -1.65  | 0.10    |
|                                        | B     | 69.42 ± 4.84|            |         |
| Sex                                    | A     | Male        | Χ² = 0.96  | 0.33    |
|                                        |       | Female      |            |         |
|                                        | B     | Male        |            |         |
|                                        |       | Female      |            |         |
| Grade of cataract (LOCS III)           | A     | Grade 1     | Χ² = 1.02  | 0.80    |
|                                        |       | Grade 2     |            |         |
|                                        |       | Grade 3     |            |         |
|                                        |       | Grade 4     |            |         |
|                                        | B     | Grade 1     |            |         |
|                                        |       | Grade 2     |            |         |
|                                        |       | Grade 3     |            |         |
|                                        |       | Grade 4     |            |         |

Values are presented as number (%) unless otherwise indicated.

LOCS = Lens Opacities Classification System.

### Table 2. Comparison of postoperative BCVA between the groups

| BCVA                | Group A | Group B | Statistics                        |
|---------------------|---------|---------|-----------------------------------|
| On POD 1            |         |         |                                   |
| >20 / 32            | 80 (82.5) | 82 (83.7) |                                   |
| 20 / 40–20 / 80     | 10 (10.3) | 8 (8.2)   |                                   |
| <20 / 80            | 7 (7.2)   | 8 (8.2)   |                                   |
| Mean logMAR         | 0.183    | 0.194    | Mann-Whitney U-test Z = -0.103, p = 0.9203 |
| Total               | 97       | 98       |                                   |
| On POD 7            |         |         |                                   |
| >20 / 32            | 87 (89.7) | 88 (89.8) |                                   |
| 20 / 40–20 / 80     | 7 (7.2)   | 8 (8.2)   |                                   |
| <20 / 80            | 3 (3.1)   | 2 (2.0)   |                                   |
| Mean logMAR         | 0.131    | 0.137    | Mann-Whitney U-test Z = 0.890, p = 0.3735 |
| Total               | 97       | 98       |                                   |
| On POD 30           |         |         |                                   |
| >20 / 32            | 88 (90.7) | 92 (93.9) |                                   |
| 20 / 40–20 / 80     | 6 (6.2)   | 5 (5.1)   |                                   |
| <20 / 80            | 3 (3.1)   | 1 (1.0)   |                                   |
| Mean logMAR         | 0.109    | 0.104    | Mann-Whitney U-test Z = 0.576, p = 0.5619 |
| Total               | 97       | 98       |                                   |

Values are presented as number (%) unless otherwise indicated.

BCVA = best-corrected visual acuity; POD = postoperative day; logMAR = logarithm of the minimum angle of resolution.
groups also showed no statistical difference with p-values of day 1 ($p = 0.54$) and day 7 ($p = 0.84$). At day 30, patients in both groups had no signs of conjunctival congestion.

Similarly, comparison of corneal edema in both the groups showed no statistical difference with $p$-values of day 1 ($p = 0.68$) and day 7 ($p = 0.55$). At day 30, patients in both groups had no evidence of corneal edema.

There was no statistical difference in the mean pain scores between the two groups (1.55 vs. 1.75 in group A and B respectively, $p = 0.139$, Mann-Whitney test) at day 1 of surgery while at day 7, mean pain score was significantly lower in the nepafenac group (0.79 vs. 1.06 in group A and B respectively, $p = 0.018$).

**CMT**

The difference in the mean CMT between the two groups at day 30 was found to be statistically significant (205.713 ± 17.14 vs. 220.984 ± 32.83 in group A and B respectively, $p < 0.001$).

**Discussion**

Phacoemulsification has emerged as the most preferred technique of cataract surgery globally [4]. Conventional phacoemulsification can be performed with an incision size of 2.8 to 3.2 mm. However, newer advances in the surgical techniques and surgical instruments combined with the arrival of newer foldable intraocular lens designs have paved the way for MICS. MICS has incision size below 2.2 mm. MICS can be either bimanual or co-axial. Irrigation, aspiration, and emulsification are all performed with the same probe through a single port in coaxial MICS. MICS has several advantages over conventional phacoemulsification technique which include a lesser degree of surgically induced astigmatism, rapid healing of the wound, better postoperative vision, and better and stable biomechanics of the corneal section [16-21]. In our study, coaxial MICS was performed in all cases. Nonetheless, despite the newer surgical innovations, some degree of intraocular inflammation is inevitable. The inflammatory reaction may be exaggerated in diabetics, poor mydriasis, pre-existing uveitis, hard cataracts, pseudoexfoliation, intra-operative complications like posterior capsular rupture [4,22,23]. In our study, we had excluded all patients who had any of the risk factors for exaggerated postoperative inflammatory response. For all patients, we evaluated lid edema, corneal edema, conjunctival hyperemia, AC cells and flare, Pain score and IOP for a month during the postoperative period as markers of early postoperative inflammation.

Inflammatory mediators produced following surgical

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**Table 3. Comparison of parameters of inflammation between both the groups**

|                      | Day 1                | Day 7                | Day 30               |
|----------------------|----------------------|----------------------|----------------------|
|                      | Group A | Group B | Group A | Group B | Group A | Group B |
| Mean score of lid edema | 0.515   | 0.469   | 0.155   | 0.204   | 0.0     | 0.0     |
|                      | Mann-Whitney U-test $Z = -0.401, p = 0.6892$ | Mann-Whitney U-test $Z = 0.188, p = 0.8493$ | - | - |
| Mean score of corneal edema | 0.247   | 0.194   | 0.072   | 0.041   | 0.0     | 0.0     |
|                      | Mann-Whitney U-test $Z = -0.401, p = 0.6892$ | Mann-Whitney U-test $Z = 0.590, p = 0.5552$ | - | - |
| Mean score of conjunctival hyperemia | 0.690   | 0.806   | 0.268   | 0.316   | 0.0     | 0.0     |
|                      | Mann-Whitney U-test $Z = 0.610, p = 0.5419$ | Mann-Whitney U-test $Z = 0.188, p = 0.8493$ | - | - |
| Mean score of AC cells | 0.57     | 0.50    | 0.04    | 0.03    | 0.0     | 0.0     |
|                      | Mann-Whitney U-test $p = 0.62$ | Mann-Whitney U-test $p = 0.8493$ | - | - |
| Mean score of AC flare | 0.43    | 0.34    | 0.0     | 0.0     | 0.0     | 0.0     |
|                      | Mann-Whitney U-test $p = 0.42$ | Mann-Whitney U-test $p = 0.8493$ | - | - |
trauma comprise of oxygen-free radicals, proteolytic enzymes, and arachidonic acid metabolites of cyclooxygenase and lipoxygenase enzymes. These mediators are responsible for the breach in the blood-aqueous barrier [1]. Both steroids and NSAIDs exhibit their anti-inflammatory properties via inhibition of the cyclooxygenase pathway of the arachidonic acid cascade. Steroids additionally inhibit the lipoxygenase pathway as well [1]. Nepafenac or amfenac amide is a potent inhibitor of both cyclooxygenase 1 and cyclooxygenase 2. It is a prodrug and can, therefore, rapidly permeate across the cornea. Nepafenac then undergoes bioactivation to its active form amfenac via deamination by hydrolases in the ocular tissues of the ciliary body, retina and choroid [5,23-25].

Corticosteroids have been used for long as the first-choice agent in all ocular surgeries for prevention or treatment of inflammation. However, steroid usage may be associated with delayed wound healing, raised IOP or an increased risk of infection. The potential for a specific topical ocular corticosteroid to raise IOP depends on its pharmacokinetics, e.g., tissue penetration, ocular bioavailability, half-life, dosage and treatment duration. Differences in the potency between the ocular corticosteroids is also a factor responsible for their differential IOP-elevating potential. The introduction of topical NSAID eye drops offers to overcome these shortcomings of topical steroids. Besides, they may provide some distinct added advantages as well over the topical steroids [4,8,22,26]. Historically, the use of topical NSAIDs is multi-dimensional. They have been used to prevent intraoperative miosis, for pain relief in refractive surgeries and prevention as well as treatment of postoperative CME [22,27-32].

Effect of NSAIDs in controlling postoperative inflammation has been studied extensively in various studies. Sahu et al. [4] evaluated the effect of topical ketorolac 0.4% (Acular LS, Allergan India), bromfenac 0.09% (Megabrom, Sun Pharmaceutical Industries, India), and nepafenac 0.1% (Nevanac) in terms of inhibiting postoperative inflammation following phacoemulsification. Nepafenac was found to be significantly more effective than the other drugs in reducing AC flare measured by laser flare photometry. In another study by Solomon et al. [22], ketorolac was found to be significantly more effective than the control drug vehicle in reducing AC cells ($p < 0.002$) and flare ($p < 0.009$), conjunctival congestion ($p < 0.010$), photophobia ($p < 0.027$), and pain ($p < 0.043$). Bucci and Waterbury [33] in another study compared the efficacy of different topical NSAIDs in the inhibition of prostaglandin E2. They concluded that ketorolac 0.45% could achieve greater inhibition of prostaglandin E2 in comparison to nepafenac 0.1% and bromfenac 0.09% when used during cataract surgery for controlling postoperative inflammation.

In our study, we had compared 0.1% nepafenac alone with 1% prednisolone in controlling postoperative inflammation. Results of our study show that nepafenac and prednisolone are almost equally effective in their anti-inflammatory actions. There was no statistical difference ($p > 0.05$) between the two groups in the grade of AC cells and flare, conjunctival hyperemia, lid edema, corneal edema and IOP during all visits in the first postoperative month. Nagpal et al. [6] had compared topical nepafenac 0.1% to prednisolone acetate 1% as postoperative anti-inflammatory agent after small gauge vitrectomies. Their study results also demonstrated no significant difference in AC inflammation ($p > 0.05$) or adnexal inflammation ($p > 0.05$) between the groups. Similar studies by Miyake et al. [5] and Miyake et al. [34] also showed no significant difference between nepafenac and fluorometholone in control of AC inflammation.

Mean pain severity score ($p = 0.018$) in our study was, however, significantly lower in the nepafenac group at 1 week following surgery. This can be explained by an additional analgesic effect of the active metabolite amfenac produced by the deamination of nepafenac [10]. In a study conducted by Naithani et al. [35], nepafenac showed better results in controlling postoperative pain following vitreoretinal surgery similar to our study. In a study by Lane et al. [23], topical nepafenac was shown to cause an unequivocal decrease in postoperative pain and inflammation. Nepafenac group had a higher percentage of pain-free patients ($p < 0.0001$) and also lower mean scores of AC cells and flare at all visits ($p < 0.0001$) compared with the control group.

In our study, the mean CMT at one month was lower in the nepafenac group compared to the steroid group and the difference was statistically significant ($205.713 \pm 17.14$ in NSAID group vs. $220.984 \pm 32.83$ in the steroid group, $p \leq 0.001$). Few other studies had compared NSAIDs with topical steroids for control of postsurgical CME and have reported significant difference in the results between the two treatment groups akin to our study results [4,6,34,36-38]. Miyake et al. [34] compared diclofenac sodium 0.1% with
fluorometholone 0.1% in controlling CME and disruption of the blood-aqueous barrier following cataract surgery. Throughout the first 8 weeks in the study, CME was present in 5.7% eyes receiving NSAID eye drops versus 54.7% eyes on steroid eye drops ($p = 0.001$). In another subsequent study by Miyake et al. [5], nepafenac 0.1% eye drops were compared with fluorometholone 0.1% eye drops for control of CME after phacoemulsification. Throughout the first 5 weeks of surgery, nepafenac was found to be more effective than fluorometholone in preventing CME. At 5 weeks of surgery, fluorescein angiographic CME incidence was also significantly lower in the NSAID group (14.3%) than in the steroid group (81.5%) ($p \leq 0.001$). The CMT was lower in the nepafenac group than in the fluorometholone group at 2 weeks ($p = 0.026$) and 5 weeks ($p = 0.005$). Results of these studies are, therefore, similar to the outcomes in our study in terms of comparison of macular thickness between the NSAID and steroid eye drops groups.

Topical steroids as already discussed before can cause undesirable side effects such as raised IOP, delayed wound healing, increased chances of infection, etc. [8]. Topical nepafenac can also cause rare side effects like punctate keratitis, corneal infiltrates, epithelial defects, etc. as reported in previous studies [39]. In our study, however, we did not notice any side effects of topical nepafenac during the study period.

In conclusion, nepafenac and prednisolone eye drops are equally efficacious in controlling postoperative inflammation following micro-incisional cataract surgery. Control of pain and prevention of CME may be slightly better with nepafenac in comparison to a topical steroid at 1-month period. Therefore, 0.1% nepafenac eye drops can be used as a stand-alone anti-inflammatory agent in uncomplicated MICS. However, our study follow-up period was for 1 month only. Longer prospective follow up studies are needed to confirm the beneficial effects of NSAIDs in the prevention of delayed postoperative CME. Nepafenac may be particularly useful in cases with glaucoma, steroid responders or those at high risk of postoperative infection due to topical steroids. It can also be beneficial as an adjunct drop during steroid tapering in cases where steroids are indicated only in the early postoperative period [6].

Our study is the first prospective randomized study to the best of our knowledge which compares the efficacy of nepafenac alone versus prednisolone alone in controlling postoperative inflammation following micro-incisional cataract surgery.

**Conflict of Interest**

No potential conflict of interest relevant to this article was reported.

**References**

1. El-Harazi SM, Feldman RM. Control of intra-ocular inflammation associated with cataract surgery. *Curr Opin Ophthalmol* 2001;12:4-8.
2. Kato K, Miyake K, Hirano K, Kondo M. Management of postoperative inflammation and dry eye after cataract surgery. *Cornea* 2019;38 Suppl 1:S25-33.
3. Bardoloi N, Sarkar S, Pilania A, Das H. Efficacy and safety of dropless cataract surgery. *Indian J Ophthalmol* 2020;68:1081-5.
4. Sahu S, Ram J, Bansal R, et al. Effect of topical ketorolac 0.4%, nepafenac 0.1%, and bromfenac 0.09% on postoperative inflammation using laser flare photometry in patients having phacoemulsification. *J Cataract Refract Surg* 2015;41:2043-8.
5. Miyake K, Ota I, Miyake G, Numaga J. Nepafenac 0.1% versus fluorometholone 0.1% for preventing cystoid macular edema after cataract surgery. *J Cataract Refract Surg* 2011;37:1581-8.
6. Nagpal M, Lambat S, Mehrotra N, et al. Topical nepafenac 0.1% alone versus prednisolone acetate 1% as postoperative anti-inflammatory agents in small gauge vitrectomy. *Indian J Ophthalmol* 2014;62:606-9.
7. DeCroos FC, Afshari NA. Perioperative antibiotics and anti-inflammatory agents in cataract surgery. *Curr Opin Ophthalmol* 2008;19:22-6.
8. Heier JS, Topping TM, Baumann W, et al. Ketorolac versus prednisolone versus combination therapy in the treatment of acute pseudophakic cystoid macular edema. *Ophthalmology* 2000;107:2034-8.
9. Chinchurreta Capote AM, Lorenzo Soto M, et al. Comparative study of the efficacy and safety of bromfenac, nepafenac and diclofenac sodium for the prevention of cystoid macular edema after phacoemulsification. *Int J Ophthalmol* 2018;11:1210-6.
10. Yuksel B, Karti O, Kusbeci T. Topical nepafenac for prevention of post-cataract surgery macular edema in diabetic patients: patient selection and perspectives. *Clin Ophthalmol* 2017;11:2183-90.

11. Chylack LT Jr, Wolfe JK, Singer DM, et al. The lens opacities classification system III. The longitudinal study of cataract study group. *Arch Ophthalmol* 1993;111:831-6.

12. Vasavada AR, Desai JP. Stop, chop, chop, and stuff. *J Cataract Refract Surg* 1996;22:526-9.

13. Vasavada A, Singh R. Step-by-step chop in situ and separation of very dense cataracts. *J Cataract Refract Surg* 1998;24:156-9.

14. Bardoloi N, Sarkar S, Pilania A, Das H. Pure phaco: phacoemulsification without ophthalmic viscosurgical devices. *J Cataract Refract Surg* 2020;46:174-8.

15. Jabs DA, Nussenblatt RB, Rosenbaum JT; Standardization of Uveitis Nomenclature (SUN) Working Group. Standardization of uveitis nomenclature for reporting clinical data. Results of the First International Workshop. *Am J Ophthalmol* 2005;140:509-16.

16. Fu C, Chu N, Yu X, Yao K. Bimanual microincision cataract surgery versus coaxial microincision cataract surgery: a meta-analysis of randomized controlled trials and cohort studies. *J Ophthalmol* 2017;2017:3737603.

17. Shentu X, Zhang X, Tang X, Yu X. Coaxial microincision cataract surgery versus standard coaxial small-incision cataract surgery: a meta-analysis of randomized controlled trials. *PLoS One* 2016;11:e0146676.

18. Luo L, Lin H, He M, et al. Clinical evaluation of three incision size-dependent phacoemulsification systems. *Am J Ophthalmol* 2012;153:831-9.

19. Can I, Takmaz T, Yildiz Y, et al. Coaxial, microcoaxial, and biaxial microincision cataract surgery: prospective comparative study. *J Cataract Refract Surg* 2010;36:740-6.

20. Wilczynski M, Supadye E, Piotr L, et al. Comparison of surgically induced astigmatism after coaxial phacoemulsification through 1.8 mm microincision and bimanual phacoemulsification through 1.7 mm microincision. *J Cataract Refract Surg* 2009;35:1563-9.

21. Alió JL, Rodriguez-Prats JL, Vianello A, Galal A. Visual outcome of microincision cataract surgery with implantation of an Acri. Smart lens. *J Cataract Refract Surg* 2005;31:1549-56.

22. Solomon KD, Cheetham JK, DeGryse R, et al. Topical ketorolac tromethamine 0.5% ophthalmic solution in ocular inflammation after cataract surgery. *Ophthalmology* 2001;108:331-7.

23. Lane SS, Modi SS, Lehmann RP, Holland EJ. Nepafenac ophthalmic suspension 0.1% for the prevention and treatment of ocular inflammation associated with cataract surgery. *J Cataract Refract Surg* 2007;33:53-8.

24. Ke TL, Graff G, Spellman JM, Yanni JM. Nepafenac, a unique nonsteroidal prodrug with potential utility in the treatment of trauma-induced ocular inflammation: II. In vitro bioactivation and permeation of external ocular barriers. *Inflammation* 2000;24:371-84.

25. Walters T, Raizman M, Ernest P, et al. In vivo pharmacokinetics and in vitro pharmacodynamics of nepafenac, amfenac, ketorolac, and bromfenac. *J Cataract Refract Surg* 2007;33:1539-45.

26. Simone JN, Whitacre MM. Effects of anti-inflammatory drugs following cataract extraction. *Curr Opin Ophthalmol* 2001;12:63-7.

27. Keates RH, McGowan KA. Clinical trial of flurbiprofen to maintain pupillary dilation during cataract surgery. *Ann Ophthalmol* 1984;16:919-21.

28. Gwon A, Vaughan ER, Cheetham JK, DeGryse R. Ocufen (flurbiprofen) in the treatment of ocular pain after radial keratotomy. *CLA O J* 1994;20:131-8.

29. Stark WJ, Fagadau WR, Stewart RH, et al. Reduction of pupillary constriction during cataract surgery using suprafen. *Arch Ophthalmol* 1986;104:364-6.

30. Keates RH, McGowan KA. The effect of topical indomethacin ophthalmic solution in maintaining mydriasis during cataract surgery. *Ann Ophthalmol* 1984;16:1116-21.

31. Koay P. The emerging roles of topical non-steroidal anti-inflammatory agents in ophthalmology. *Br J Ophthalmol* 1996;80:480-5.

32. Arshinoff S, D’Addario D, Sadler C, et al. Use of topical nonsteroidal anti-inflammatory drugs in excimer laser photorefractive keratectomy. *J Cataract Refract Surg* 1994;20 Suppl:216-22.

33. Bucci FA Jr, Waterbury LD. Prostaglandin E2 inhibition of ketorolac 0.45%, bromfenac 0.09%, and nepafenac 0.1% in patients undergoing phacoemulsification. *Adv Ther* 2011;28:1089-95.

34. Miyake K, Masuda K, Shirato S, et al. Comparison of diclofenac and fluorometholone in preventing cystoid macular edema after small incision cataract surgery: a multicentered prospective trial. *Jpn J Ophthalmol* 2000;44:58-67.

35. Naithani P, Puranik S, Vashisht N, et al. Role of topical
nepafenac in prevention and treatment of macular edema after vitreoretinal surgery. *Retina* 2012;32:250-5.

36. Flach AJ, Jaffe NS, Akers WA. The effect of ketorolac tromethamine in reducing postoperative inflammation: double-mask parallel comparison with dexamethasone. *Ann Ophthalmol* 1989;21:407-11.

37. Simone JN, Pendelton RA, Jenkins JE. Comparison of the efficacy and safety of ketorolac tromethamine 0.5% and prednisolone acetate 1% after cataract surgery. *J Cataract Refract Surg* 1999;25:699-704.

38. Brennan KM, Brown RM, Roberts CW. A comparison of topical non-steroidal anti-inflammatory drugs to steroids for control of post cataract inflammation. *Insight* 1993;18:8-9.

39. Gaynes BI, Fiscella R. Topical nonsteroidal anti-inflammatory drugs for ophthalmic use: a safety review. *Drug Saf* 2002;25:233-50.