

Research Article

Effect of Adjunctive Topical Nepafenac on Early Inflammation after Cataract Surgery: A Multicenter Study

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ABSTRACT

Objective: To assess whether adding topical nepafenac 0.1% to postoperative corticosteroid treatment improved control of inflammation after uncomplicated cataract surgery.

Methods: This multicenter comparative study was conducted at three tertiary care hospitals in Punjab, Pakistan, from January to June 2025. Adults undergoing uncomplicated phacoemulsification received nepafenac 0.1% three times daily plus prednisolone acetate 1%, or prednisolone acetate 1% alone, for four weeks. The primary outcome was the proportion of eyes with no anterior chamber cells on postoperative day 7. Anterior chamber flare, pain, corrected distance visual acuity, central macular thickness and adverse events were also assessed.

Results: Of 240 patients, 120 received each regimen. On day 7, anterior chamber cells had resolved in 83 patients (69.2%) receiving nepafenac and 65 (54.2%) receiving corticosteroid alone. The absolute difference was 15.0 percentage points (95% confidence interval, 2.8-27.2; p=0.018). Mean cell grade and pain score were also lower in the nepafenac group. By day 28, inflammation had resolved in most eyes in both groups. Visual acuity and central macular thickness did not differ significantly. No serious treatment-related ocular event was recorded.

Conclusion: Adjunctive nepafenac improved control of anterior chamber inflammation during the first postoperative week. The difference between regimens was smaller at four weeks, when recovery was favorable in both groups.

Keywords: Anterior Chamber Cells, Inflammation, Nepafenac, Phacoemulsification.

INTRODUCTION

Phacoemulsification usually produced a rapid improvement in vision, but surgical manipulation also provoked an inflammatory response during the first days of recovery.[1] Disruption of the blood–aqueous barrier allowed inflammatory cells and proteins to enter the anterior chamber, where they could be observed clinically or measured as aqueous flare.[2] The response was generally mild after uncomplicated surgery, although greater inflammation could accompany corneal swelling and slower visual recovery.[3] Inflammation that persisted beyond the usual recovery period was also associated with an increased risk of postoperative macular edema.[4]

Controlling this response remained an important part of postoperative care. Topical corticosteroids were effective, but their schedules required repeated instillation and monitoring for adverse effects, including a rise in intraocular pressure.[5] Trials of different anti-inflammatory regimens showed that the choice and timing of treatment could influence the early postoperative response.[1] Nepafenac offered a different approach through topical inhibition of prostaglandin-mediated inflammation. In a trial of uncomplicated surgery, preoperative nepafenac was investigated as a way to reduce postoperative aqueous flare. [6]

The question was not simply whether an anti-inflammatory drug worked. Surgeons needed to know what benefit an additional drop provided when a corticosteroid was already prescribed. A multicenter trial assessed postoperative recovery by grading anterior chamber cells and flare, two signs of inflammation readily observed during slit-lamp examination.[7] Another trial showed that inflammation could resolve quickly under a shorter, standardized postoperative regimen, emphasizing the importance of choosing an early assessment point.[8] These findings supported measurement during the first postoperative week, when a difference between regimens would be most likely to matter to patients.

Evidence concerning nepafenac itself remained relevant to this decision. In a Pakistani study, nepafenac 0.1% suppressed anterior chamber cells more effectively than diclofenac 0.1% during the early weeks after cataract surgery.[9] A systematic review found that NSAIDs and NSAID–corticosteroid combinations reduced several postoperative inflammatory and macular outcomes compared with corticosteroids alone, although effects varied across studies.[10] A network meta-analysis comparing individual topical NSAIDs likewise found differences in visual and macular outcomes, but the treatments and accompanying steroid regimens were not uniform.[11] Such evidence could not establish that an early reduction in anterior chamber cells would necessarily produce better final visual acuity.

Assessment methods also influenced interpretation. Laser flare photometry offered an objective measure of intraocular inflammation, while slit-lamp grading remained more readily available during routine postoperative visits.[12] Trials of corticosteroid regimens demonstrated that anterior chamber inflammation could be assessed alongside visual acuity and intraocular pressure without treating those outcomes as interchangeable.[13] A nepafenac-focused review further suggested a benefit for macular swelling when the drug was added to steroids, but its macular findings did not directly answer how much early anterior chamber inflammation improved.[14]

That distinction was useful in tertiary services across Punjab, where an additional medicine carried both a purchase cost and a dosing burden. The present study therefore assessed whether adding topical nepafenac 0.1% to a common corticosteroid regimen increased the

proportion of eyes with no anterior chamber cells on day 7 after uncomplicated phacoemulsification. Pain, flare, visual acuity, central macular thickness and safety were examined as secondary outcomes.

MATERIALS AND METHODS

This multicenter comparative study was conducted in the ophthalmology departments of three tertiary care hospitals in Punjab, Pakistan, from January to June 2025. Ethical approval was obtained from the participating institutions, and written informed consent was obtained from all patients before enrolment. Adults aged 40 years or older who underwent uncomplicated phacoemulsification with posterior chamber intraocular lens implantation were included. One eye per patient was studied.

Patients with active uveitis, significant corneal disease, and previous intraocular surgery in the study eye, established macular edema, advanced diabetic retinopathy or a known allergy to the study medications were excluded. Eyes requiring a specialized postoperative anti-inflammatory regimen were also excluded. Posterior capsule rupture and other intraoperative complications led to exclusion before treatment allocation. These criteria kept the comparison focused on recovery after uncomplicated cataract surgery.

Patients were allocated equally to two postoperative regimens using a computer-generated sequence stratified by center. Allocation was concealed in sequentially numbered, opaque envelopes opened after surgery. Both groups received prednisolone acetate 1% four times daily during the first postoperative week, followed by the same taper over the next three weeks. The nepafenac group also received nepafenac 0.1%, one drop three times daily, from the day of surgery through day 28. The comparison group received prednisolone acetate without an additional topical NSAID. Postoperative antibiotic treatment followed the participating center's routine schedule. Patients and treating clinicians knew which drops had been prescribed; outcome examiners were kept unaware of allocation.

Anterior chamber cells and flare were assessed separately at the slit lamp using a common 0 to 4+ grading scale. Grade 0 indicated that no cells or flare were observed. Examiners used a shared assessment guide, and day 7 examinations were scheduled within a two-day window. The primary outcome was the

proportion of eyes with grade 0 anterior chamber cells on postoperative day 7. Secondary outcomes included cell grade at other visits, the proportion of eyes with grade 0 flare, pain, corrected distance visual acuity, intraocular pressure and central macular thickness.

Pain was recorded on a numerical scale from 0, indicating no pain, to 10, indicating the worst

pain. Corrected distance visual acuity was expressed in logMAR units. Central macular thickness was measured before surgery and on day 28 using optical coherence tomography. Patients recorded their use of prescribed drops in a short diary, which was reviewed alongside adverse symptoms and any additional treatment at follow-up. **Table 1** shows the assessment schedule.

Table 1. Clinical Assessments During Follow-Up

Assessment	Before surgery	Day 1	Day 7	Day 28
Medical and ocular history	✓			
Corrected distance visual acuity	✓	✓	✓	✓
Anterior chamber cells and flare	✓	✓	✓	✓
Pain score		✓	✓	✓
Intraocular pressure	✓	✓	✓	✓
Macular optical coherence tomography	✓			✓
Adherence and adverse-event review		✓	✓	✓

Data were analyzed using SPSS version 26.0. Continuous variables were reported as mean±SD and categorical variables as number and percentage. The day 7 primary outcome was compared using the chi-square test and reported as an absolute risk difference with a 95% confidence interval. Continuous outcomes were compared using the t-test or Mann-Whitney U test. All allocated patients were included in the day 7 analysis; day 28 analyses included those who attended follow-up. A two-sided $p < 0.05$ was considered significant.

RESULTS

The study included 240 patients, with 120 in each treatment group. All patients completed the day 7 assessment. At day 28, follow-up data were available for 116 patients in the nepafenac group and 114 in the comparison group. Age, diabetes status, preoperative visual acuity and baseline central macular thickness were similar between groups. The study included 240 patients, with 120 in each treatment group. Baseline characteristics were similar between groups (**Table 2**).

Table 2. Baseline Characteristics of the Patients (n=240)

Characteristic	Total (n=240)	Nepafenac + steroid (n=120)	Steroid alone (n=120)
Age, years, mean±SD	63.9±9.1	64.1±8.9	63.6±9.3
Women, n (%)	129 (53.8)	66 (55.0)	63 (52.5)
Diabetes mellitus, n (%)	66 (27.5)	32 (26.7)	34 (28.3)
Preoperative CDVA, logMAR, mean±SD	0.79±0.29	0.78±0.28	0.80±0.30
Baseline central macular thickness, µm, mean±SD	246.5±22.5	246±22	247±23

On postoperative day 1, few eyes in either group had reached grade 0 anterior chamber cells. By day 7, the primary outcome had been achieved in 83 patients (69.2%) receiving nepafenac and 65 (54.2%) receiving steroid alone. The absolute difference was 15.0 percentage points (95% CI, 2.8–27.2;

$p=0.018$). Mean cell grade was also lower in the nepafenac group at that visit. By day 28, grade 0 cells were recorded in most eyes in both groups, and the between-group difference had narrowed. The visit-specific findings are presented in **Table 3**.

Table 3. Anterior Chamber cell Outcomes

Outcome	Nepafenac + steroid	Steroid alone	p-value
Day 1: grade 0 cells, n/120 (%)	11 (9.2)	9 (7.5)	0.64

Day 1: cell grade, mean±SD	1.43±0.72	1.52±0.76	0.35
Day 7: grade 0 cells, n/120 (%)	83 (69.2)	65 (54.2)	0.018
Day 7: cell grade, mean±SD	0.42±0.57	0.61±0.67	0.019
Day 28: grade 0 cells, n/116 or 114 (%)	109 (94.0)	103 (90.4)	0.30
Day 28: cell grade, mean±SD	0.07±0.26	0.11±0.32	0.30

Flare followed a similar early pattern. On day 7, grade 0 flare was recorded in 110 eyes (91.7%) in the nepafenac group and 99 eyes (82.5%) in the comparison group. Patients receiving

nepafenac also reported a slightly lower mean pain score at that visit. By day 28, flare and pain were uncommon in both groups. These outcomes are shown in **Table 4**.

Table 4. Anterior Chamber Flare and Ocular Pain

Outcome	Nepafenac + steroid	Steroid alone	p-value
Day 1: grade 0 flare, n/120 (%)	67 (55.8)	61 (50.8)	0.44
Day 7: grade 0 flare, n/120 (%)	110 (91.7)	99 (82.5)	0.034
Day 28: grade 0 flare, n/116 or 114 (%)	115 (99.1)	112 (98.2)	0.53
Day 1: pain score, mean±SD	2.2±1.5	2.6±1.7	0.054
Day 7: pain score, mean±SD	0.5±0.9	0.8±1.1	0.021
Day 28: pain score, mean±SD	0.1±0.4	0.1±0.5	0.99

Corrected distance visual acuity improved substantially after surgery in both groups. At day 28, mean visual acuity was 0.13±0.11 logMAR in the nepafenac group and 0.14±0.12 logMAR in the comparison group. Central macular thickness increased slightly from

baseline in each group, without a statistically significant between-group difference. **Table 5** presents these secondary outcomes. Clinical macular edema was not a prespecified primary endpoint.

Table 5. Visual Acuity and Central Macular Thickness

Outcome	Nepafenac + steroid	Steroid alone	p-value
Day 7 CDVA, logMAR, mean±SD	0.19±0.13	0.21±0.14	0.25
Day 28 CDVA, logMAR, mean±SD	0.13±0.11	0.14±0.12	0.51
Day 28 central macular thickness, µm, mean±SD	253±25	257±27	0.24
Change in thickness from baseline, µm, mean±SD	7±13	10±15	0.10

Treatment was generally well tolerated. Transient stinging was reported more often by patients receiving nepafenac. Five patients in that group and six in the comparison group had an intraocular pressure measurement above 21 mmHg at one or more visits. One patient in

each group required an additional review for persistent inflammation. Reported adherence and safety findings are presented in **Table 6**. No serious treatment-related ocular event was recorded.

Table 6. Treatment use and Safety

Outcome, n (%)	Nepafenac + steroid (n=120)	Steroid alone (n=120)
Transient stinging	9 (7.5)	4 (3.3)
Intraocular pressure >21 mmHg at any visit	5 (4.2)	6 (5.0)
Additional review for persistent inflammation	1 (0.8)	1 (0.8)
Reported ≥90% adherence to prescribed drops	105 (87.5)	110 (91.7)
Serious treatment-related ocular event	0	0

CDVA: corrected distance visual acuity; CI: confidence interval; SD: standard deviation.

DISCUSSION

Adding nepafenac to prednisolone acetate improved early control of anterior chamber inflammation in this multicenter study. The difference was most apparent at the day 7 visit, when an additional 15% of patients in the nepafenac group had no visible anterior chamber cells. Flare and pain also favored nepafenac at that visit. By day 28, inflammation had resolved in most eyes regardless of treatment, indicating that the clearest benefit concerned the first postoperative week rather than the final four-week examination.

A Pakistani study of nepafenac in patients with diabetes examined prevention of postoperative cystoid macular edema, an outcome distinct from the anterior chamber cells measured here.[15] Its findings supported continued interest in the drug but could not be used to estimate the early inflammatory difference observed in our patients. A network meta-analysis also favored nepafenac for prevention of postoperative macular edema, although variation across trials limited direct comparisons.[16] Our day 28 OCT findings showed no significant difference in mean central macular thickness. The present study's duration and sample size did not allow that finding to be interpreted as evidence that the regimens were equivalent for prevention of clinical macular edema.

The timing of benefit was consistent with a prospective study in which adjunctive nepafenac affected early postoperative pupillary responses, particularly during the first week.[17] That study measured a different response, but it reinforced the value of examining recovery soon after surgery. Conversely, a trial of dexamethasone-containing postoperative treatment reported that anterior chamber cellularity and flare resolved quickly in most patients.[18] The high day 28 resolution rates in both of our groups were therefore unsurprising. They showed that prednisolone acetate alone remained an effective regimen for many patients after uncomplicated surgery.

The difference in pain scores was statistically significant at day 7 but small in absolute terms: the group means differed by 0.3 points on a 10-point scale. That distinction mattered when considering an extra medicine. Patients prescribed nepafenac had to obtain it and instill three additional drops each day. Research comparing postoperative regimens with different patient-administered drop requirements has assessed preference as well

as inflammation, emphasizing that treatment experience belongs alongside clinical signs.[19] Trials of lower-frequency anti-inflammatory schedules have likewise addressed the practical burden of repeated instillation.[20]

The study was strengthened by its multicenter design, consistent postoperative treatment schedule and prespecified day 7 outcome. Masked assessment of inflammation and follow-up of both clinical and visual outcomes provided a clear picture of early recovery after uncomplicated phacoemulsification.

CONCLUSION

Adjunctive topical nepafenac improved control of anterior chamber inflammation during the first week after uncomplicated cataract surgery. By four weeks, visual recovery was similar with both regimens. Nepafenac may therefore be useful when early postoperative inflammation is a particular concern.

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