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Original Research Article

COMPARATIVE EVALUATION OF TOPICAL NEPAFENAC, FLURBIPROFEN, AND BROMFENAC IN PERIOPERATIVE MANAGEMENT OF CATARACT SURGERY

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Abstract

Background: Cataract surgery is the most frequently performed ophthalmic surgery worldwide, yet intraoperative miosis and postoperative inflammation represent obstacles to successful surgical outcomes. Nonsteroidal anti-inflammatory agents likes NSAIDs in the form of Nepafenac, Flurbiprofen and Bromfenac are used to overcome this issue, but little data on comparison are available in the Indian population.

Objective: To compare the effectiveness and safety of topical Nepafenac 0.1%, Flurbiprofen 0.03%, and Bromfenac 0.09% in maintaining intraoperative mydriasis and controlling postoperative inflammation in patients undergoing phacoemulsification cataract surgery.

Materials and Methods: The study was conducted at Department of Ophthalmology of Era's Lucknow Medical College and Hospitals. It was a prospective randomized comparative study enrolling 300 patients undergoing cataract surgery, which includes an equal number of patients allocated into 3 groups and received Nepafenac, Flurbiprofen and Bromfenac perioperatively. Pupillary size was measured intraoperatively at beginning of surgery, during surgery, and at the end of surgery. Anterior chamber inflammation was recorded on days 1 and 7 postoperatively. Adverse events and visual acuity were all documented.

Results: The mean decrease in pupillary diameter beginning of surgery to end of surgery was significantly less in both the Nepafenac (1.0 ± 0.4 mm) and Bromfenac (0.9 ± 0.3 mm) groups than in the Flurbiprofen group (1.8 ± 0.5 mm) ($p < 0.001$). The anterior chamber cell and flare scores at postoperative days 1 and 7 were found to be significantly lower in the Nepafenac and Bromfenac groups ($p < 0.001$), signifying better inflammation control. At 1 week, visual acuity had improved significantly in all groups, with no between-group differences being statistically significant. All medications were well tolerated, and minimal mild ocular discomfort was experienced, nol serious adverse events were documented.

Conclusions: Nepafenac and Bromfenac are more effective than Flurbiprofen to maintain intraoperative mydriasis and postoperative control of inflammation, and have similar safety profiles. These results favour their preference in the perioperative management of cataract surgeries in Indian clinical practice.

Keywords: Cataract surgery, Nepafenac, Flurbiprofen, Bromfenac, Intraoperative mydriasis, Postoperative inflammation, Nonsteroidal anti-inflammatory drugs (NSAIDs), Phacoemulsification, India.

Introduction

Cataract is still the most prevalent cause of treatable blindness worldwide, with an estimated 51% of world blindness as per the World Health Organization (WHO) [1]. In India, alone, cataract causes about 62.6% of blindness, impacting millions of cases and acting as a serious public health matter [2]. Due to growing ageing population, demand for cataract surgery is increasing, and it is among the most frequently performed ophthalmic surgical procedure globally and in India[3].Phacoemulsification cataract surgery is the gold standard and provides excellent visual results and short recovery time. But the process is not without its problems. Intraoperative miosis and proinflammatory activity represent still key issues, that however, do not necessarily negatively affect the safety, visibility, patient's well-being, and outcomes of the surgical procedure [4]. Ensuring a good mydriasis during surgery improves the surgical approach to the lens and minimizes the risk for complications that include posterior capsule tear and iris damage [5]. Uncontrolled postoperative inflammation can result in delayed visual recovery and potential devastating complications such as cystoid macular edema (CME) that may threaten the visual outcome [6]. Nonsteroidal anti-inflammatory drugs (NSAIDs) have been used in ophthalmology extensively as inhibitors of prostaglandin synthesis - the inflammatory cascade responsible for intra-operative miosis and post operative inflammation [7]. Topical NSAIDs used in the perioperative period minimize pupil miosis and do reduce anterior chamber inflammation during the surgical process, with some benefits for the recovery process . Flurbiprofen, Nepafenac, Bromfenac, Ketorolac, Diclofenac are the commonly used NSAIDs used in topical ocular therapy with variations in potency, penetration into the ocular tissue, frequency of dosing, safety profile etc [8].Flurbiprofen, one of the first NSAIDs developed for ophthalmic use, has efficacy in preventing intraoperative miosis; however, its use has been limited by its relatively short duration of action and weaker anti-inflammatory activity in comparison to later NSAIDs [9]. Nepafenac and Bromfenac are newer NSAIDs with higher corneal penetrability and prolonged intraocular retention times, offering better cyclooxygenase-2 (COX-2) blockade and prostaglandin-induced inflammation control . It is believed that these drugs more effectively control postoperative inflammation and may reduce dependence on corticosteriods, and their related toxicity .Although these agents are widely employed, no head-to-head data are available on the relative clinical efficacy and safety of Nepafenac, Flurbiprofen, and Bromfenac in the Indian subcontinent, where various environmental factors, accessibility to healthcare and patient profile may affect clinical outcomes. The value of comparative effectiveness of these agents may also assist ophthalmologists in individualising patients' perioperative regimen in achieving the best surgical outcomes and satisfaction[10].

Hence, the present study plans to compare the perioperative use of Topical Nepafenac 0.1%, Flurbiprofen 0.03% and Bromfenac 0.09% in phacoemulsification cataract surgery, including maintaining intraoperative mydriasis; controlling postoperative inflammation along with their safety and visual outcomes. Findings from this study will be useful for applicability to clinical practice in India and other similar settings.

Materials and Methods

The study was conducted at Department of Ophthalmology of Era's Lucknow Medical College and Hospitals from January 2020 to January 2021This was a prospective, randomized, comparative clinical trial done at a tertiary eye care centre over an

year after institutional ethics committee approval. Three hundred patients with senile cataract undergoing phacoemulsification cataract surgery were included after they provided written informed consent.

Eligible patients were between 40 and 80 years of age, had no history of ocular surgery or active ocular inflammation, and met inclusion criteria. Excluding criteria were presence of known hypersensitivity to nonsteroidal anti-inflammatory drugs (NSAIDs) or other components, active ocular infection or inflammation, anamnesis of glaucoma or retinal disease, systemic administration of NSAIDs or corticosteroids within 1 week before surgery.

The patients were allocated simultaneously and equally in three groups of 100 patients according to computer generated randomization codes. Topical Nepafenac 0.1% was used in group 1, group 2 using Flurbiprofen 0.03% and group 3 using Bromfenac 0.09%. Patients received the NSAID eye drops three times daily, starting the day before surgery and continued for 1 week after surgery. Equal preoperative pupillary dilatation was achieved with 0.8% tropicamide and 5% phenylephrine instilled 30 minutes before surgery in every group.

Topical anesthesia was used for phacoemulsification and the experienced surgeons performing the surgery were all masked to the group of the patient. Pupillary diameter was measured intraoperatively at three time points (before incision, in the middle of operation, and after operation) by a caliper at the surgical microscope. Postoperative inflammation was graded by scoring anterior chamber cells and flare on days 1 and 7 postoperatively using a SUN Working Group system on slit-lamp examination. Preoperative and one week postoperative visual acuity was measured with logMAR chart. The safety evaluation was based on adverse events, including ocular discomfort, corneal edema, allergic reactions, and serious ocular complications throughout the study. Collected data were statistically analyzed. For continuous variables, mean ± standard deviation was used, and ANOVA or t-test and paired t-test were performed. Comparisons of categorical variables were made by the Chi-square test. Statistical significance was defined as having a p-value less than 0.05.

Results

Baseline Demographic and Clinical Characteristics: A total of 300 patients undergoing cataract surgery were enrolled and randomized equally into three treatment groups: Nepafenac (n = 100), Flurbiprofen (n = 100), and Bromfenac (n = 100). The groups were well-matched in terms of demographic and clinical parameters, including age, sex distribution, cataract grade, baseline pupillary diameter, and baseline visual acuity.

Table 1: Baseline demographic and clinical characteristics of patients across treatment groups

Parameter	Nepafenac (n=100)	Flurbiprofen (n=100)	Bromfenac (n=100)
Mean Age (years)	62.4 ± 8.1	63.2 ± 7.9	61.8 ± 8.3
Male/Female (n)	54 / 46	50 / 50	52 / 48
Cataract Grade (Nuclear) (%)	70 (70%)	68 (68%)	69 (69%)
Baseline Pupillary Diameter (mm)	7.8 ± 0.6	7.9 ± 0.7	7.8 ± 0.5
Baseline Visual Acuity (LogMAR)	1.2 ± 0.3	1.3 ± 0.4	1.2 ± 0.3

Data are presented as mean ± standard deviation (SD) or number (percentage). No statistically significant differences were observed among the groups (ANOVA or

Chi-square test). The absence of significant differences confirms the comparability of the groups, ensuring a reliable basis for evaluating treatment outcomes.

Intraoperative Pupillary Diameter Changes: Pupillary diameter was measured at three key surgical stages: baseline (pre-incision), mid-surgery, and end of surgery. The maintenance of mydriasis was significantly better in the Nepafenac and Bromfenac groups compared to Flurbiprofen.

Table 2: Intraoperative pupillary diameter (mm) at different surgical stages

Time Point	Nepafenac	Flurbiprofen	Bromfenac	p-value
Baseline	7.8 ± 0.6	7.9 ± 0.7	7.8 ± 0.5	0.68
Mid-Surgery	7.1 ± 0.5	6.4 ± 0.6	7.2 ± 0.4	<0.001
End of Surgery	6.8 ± 0.5	6.1 ± 0.7	6.9 ± 0.4	<0.001
Mean Reduction	1.0 ± 0.4	1.8 ± 0.5	0.9 ± 0.3	<0.001

Values are mean ± SD. Statistical analysis performed using repeated measures ANOVA with Bonferroni post-hoc correction.

Nepafenac and Bromfenac significantly reduced intraoperative miosis compared to Flurbiprofen ($p < 0.001$), suggesting better surgical field stability and potentially improved surgical outcomes.

Postoperative Anterior Chamber Inflammation: Inflammation was assessed on postoperative Days 1 and 7 using standardized grading for anterior chamber cells and flare. Both Nepafenac and Bromfenac demonstrated significantly lower inflammation scores than Flurbiprofen at both time points.

Table 3: Anterior chamber inflammation scores (cells and flare) on postoperative Days 1 and 7

Day	Parameter	Nepafenac	Flurbiprofen	Bromfenac	p-value
Day 1	Cells (Grade 0–4)	1.2 ± 0.4	1.8 ± 0.5	1.1 ± 0.3	<0.001
	Flare (Grade 0–4)	1.0 ± 0.3	1.5 ± 0.4	0.9 ± 0.3	<0.001
Day 7	Cells (Grade 0–4)	0.3 ± 0.1	0.7 ± 0.3	0.2 ± 0.1	<0.001
	Flare (Grade 0–4)	0.2 ± 0.1	0.5 ± 0.2	0.2 ± 0.1	<0.001

Data are mean ± SD. Statistical comparisons made using the Kruskal-Wallis test. Both Nepafenac and Bromfenac were significantly more effective than Flurbiprofen in controlling postoperative inflammation ($p < 0.001$), indicating superior anti-inflammatory efficacy.

Visual Acuity Outcomes: Visual acuity improved significantly in all groups by Day 7 postoperatively. However, there were no statistically significant differences in the degree of improvement among the three groups.

Table 4: Preoperative and postoperative visual acuity (LogMAR) and mean improvement

Parameter	Nepafenac	Flurbiprofen	Bromfenac	p-value
Preoperative VA	1.2 ± 0.3	1.3 ± 0.4	1.2 ± 0.3	0.51
Postoperative VA (Day 7)	0.4 ± 0.2	0.5 ± 0.2	0.4 ± 0.2	0.38
Mean Improvement	0.8 ± 0.3	0.8 ± 0.3	0.8 ± 0.2	0.97

Values are mean ± SD. Paired t-tests used for within-group comparisons; ANOVA used for between-group comparisons.

All three NSAIDs facilitated significant visual recovery post-surgery, with no significant intergroup differences in visual outcomes at one week.

Safety and Adverse Events: The incidence of adverse events was low and comparable across all treatment groups. The most common side effect was mild ocular discomfort.

No serious adverse events were reported in any group.

Table 5: Incidence of ocular adverse events during the perioperative period

Adverse Event	Nepafenac	Flurbiprofen	Bromfenac	p-value
Ocular Discomfort (%)	8 (8%)	12 (12%)	7 (7%)	0.40
Corneal Edema (%)	2 (2%)	3 (3%)	1 (1%)	0.67
Allergic Reaction (%)	0 (0%)	1 (1%)	0 (0%)	0.32
Serious Adverse Events	0	0	0	–

Data are presented as number (percentage). Statistical analysis performed using the Chi-square test.

All three drugs were safe and well tolerated, with no statistically significant differences in the incidence of adverse events.

Discussion

This was a randomized, prospective study to compare the efficacy and safety of Nepafenac, Flurbiprofen, and Bromfenac drops to maintain intraoperative mydriasis and control post cataract surgery inflammation in 300 patients. Our results show that Nepafenac and Bromfenac are better in maintaining mydriasis, and controlling the inflammation after surgery better than Flurbiprofen, with no unsafe compromise of safety.

Control of Pupil Size During Surgery: Good pupillary dilatation is essential for ideal surgical exposure and less complications during cataract surgery. Both Nepafenac and Bromfenac the groups showed significantly lesser mean reduction in pupillary diameter during surgery as compared to Flurbiprofen ($p < 0.001$) in this study. It is in accordance with other clinical trials that have reported strong mydriatic-sparing of new-generation NSAIDs such as Nepafenac and Bromfenac, due to their increased tissue penetration and greater inhibition of prostaglandin synthesis in the iris and ciliary body [10,11].Flurbiprofen was shown to be a successful drug to prevent intraoperative miosis, with relatively more induced pupillary dilation. This could be a result of its lower ocular availability, and shorter lasting effect, which restrict a prolonged inhibition of prostaglandins [12]. Maintaining mydriasis is especially crucial for complicated cases and patients with predisposing factors for intraoperative miosis, hence by choosing NSAIDS with higher effectiveness like Nepafenac or Bromfenac, could lead us to better surgical results [13].

Control of Post-Operative Inflammation: Improper treatment of postoperative inflammation can retard visual rehabilitation, and increase risk for complications such as cystoid macular edema. The anterior chamber cell and flare scores of both the Nepafenac and Bromfenac groups were significantly less than those of the Flurbiprofen group on the day 1 and 7 post-operatively ($p < 0.001$), as observed in our study. This observation is consistent with the previous reports indicating that Nepafenac and Bromfenac show more potent anti-inflammatory activities due to greater efficiency for COX-2 inhibition [14,15].Better control of inflammation provided by those drugs can

result in increased patient comfort and quicker visual recovery, and possibly less use of corticosteroids with their attendant risks of transient induced intraocular hypertension and other adverse side effects [16]. Flurbiprofen may nevertheless be less potent in postoperative inflammation reduction because of its PK properties and weaker COX2 blocking [17].

Visual Outcomes: All three groups showed significant postoperative increase in visual acuity at 1 week without any significant differences among the three teatments. This suggests that, despite pharmacological distinctions with regard to inflammation and mydriasis, the overall functional result in standard cataract surgery is outstanding with any NSAID. Longer-term follow-up may be conducted to investigate whether a more efficient control of inflammation leads to better outcomes, particularly with respect to the incidence of CME [18].

Safety and Tolerability: The rate of adverse events was low and similar between groups; mild ocular discomfort was the most commonly reported. None of them had serious adverse events or allergies. This safety profile is in line with available literature describing the tolerability of topical NSAIDs in perioperative ophthalmic surgery [19]. The favorable safety profile further supports the clinical utility of Nepafenac and Bromfenac that while of greater potency they are not unsafe

Clinical Relevance and Indian Scenario: Cataract still constitutes the leading cause of reversible blindness in India, and optimisation of the preoperative management is crucial for an increased surgical success and a better patient satisfaction [10].

Topical NSAIDs like Nepafenac, Flurbiprofen, and Bromfenac are available in India and are cost-effective; they are therefore practical options in ophthalmic practice in India. Our results have significant implications for clinical practice: it seems reasonable that Nepafenac and Bromfenac are the preferred drugs in patients with a high risk for perioperative miosis or inflammation, minimizing complications and optimizing surgical operations [19,20].

Limitations: In this study, the time point of follow-up after operation was relatively short and was 1 week. Long-term follow-up would also be useful to evaluate the effect of these NSAIDs on late inflammatory sequelae and visual results. Furthermore, cost-effectiveness and patient- reported outcome were not assessed in the study with would be highly relevant in resource-poor settings .

Conclusion

Conclusion: Nepafenac and Bromfenac were found to be more effective than Flurbiprofen in maintaining intraoperative mydriasis and postoperative inflammation control in patients undergoing cataract surgery and their safety profile was similar. Integrating these newer NSAIDs into perioperative pathways is anticipated to facilitate better surgical state and has the potential to impact patient outcome in the Indian population.

Declarations

Ethics Approval and Consent to Participate: This study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Ethics Committee of [Institution Name] (Approval No. [insert number]). Written informed consent was obtained from all participants prior to enrollment.

Consent for Publication: Not applicable. No individual person's data are presented in this manuscript.

Availability of Data and Materials: The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

Competing Interests: The authors declare that they have no competing interests.

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