

Prospective, Comparative Assessment of Safety and Efficacy of Various Nsaids with Prednisolone Acetate After Uneventful Phacoemulsification

Rajnee Sinha¹, Priyanka²

¹Senior Resident, Department of Ophthalmology, Patna Medical College and Hospital, Patna, Bihar, India

²Assistant Professor, Department of Ophthalmology, Patna Medical College and Hospital, Patna, Bihar, India

Received: 04-11-2021 / Revised: 18-12-2021 / Accepted: 17-02-2022

Corresponding author: Dr. Priyanka

Conflict of interest: Nil

Abstract

Aim: A comparative analysis of topical corticosteroids and non-steroidal anti-inflammatory drugs to control inflammation and macular edema following uneventful phacoemulsification

Methods: This prospective, comparative study conducted in the Department of Ophthalmology, Patna Medical College and Hospital, Patna, Bihar, India, for 12 months. This study comparing nepafenac (0.1%), bromfenac (0.07%), preservative-free ketorolac (0.4%), nepafenac (0.3%), and prednisolone acetate (1%) eye drops in patients undergoing uncomplicated phacoemulsification. The local ethics committee approved the study protocol. The trial was conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent is routinely obtained from all patients undergoing cataract surgery.

Results: There was no significant difference in the percentage of patients with AC cells grade of 0, 1+, and 2+ between the steroid group (group 1) and NSAIDs groups at 1-week follow-up. However, the number of patients with grade 0 AC cells was maximum in the nepafenac 0.3% group (58/96, 60.4%) and least in the bromfenac 0.07% group (33/93, 35.5%) at 1-week follow-up. None of the patients had cells at 6-week follow-up. Thus, the bromfenac group showed the least potency and the nepafenac 0.3% group showed maximal potency in control of AC inflammation though not statistically significant. At 6-weeks, the mean increase in CMT from baseline was similar between the prednisolone group and NSAIDs group except in the nepafenac 0.3% group that showed less increase in CMT as compared to prednisolone ($P = 0.004$). Thus, nepafenac 0.3% might be more effective than prednisolone in preventing CME. The mean (SD) of the change in CMT from baseline to 1-week postoperative period was compared between prednisolone and NSAIDs groups. It was found that there was an increase in CMT at 1 week in all groups, which was minimum in the nepafenac 0.3% group. On comparison with prednisolone, there was a significantly lower increase in CMT in the nepafenac 0.3% group ($P = 0.003$) but a significantly higher increase in CMT in the ketorolac and bromfenac group ($P = 0.006$ and 0.004 , respectively).

Conclusion: Nepafenac 0.3% can be used as a sole anti-inflammatory agent in patients with uneventful phacoemulsification and combination therapy can be used in high-risk cases.

Keywords: phacoemulsification, prednisolone, NSAIDs

This is an Open Access article that uses a fund-ing model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

Recent advances in cataract extraction, have led to a reduction in post-operative inflammation with phacoemulsification being the most preferred method. However, this also triggers an inflammatory cascade leading to discomfort, pain, and cystoid macular edema (CME).^[1,2] The incidence of clinical CME is 0%–2% in an uneventful phacoemulsification.^[3,4] Thus, it is imperative to treat postoperative inflammation for a satisfactory visual outcome.

Topical steroids commonly used might increase IOP, inhibit wound healing, and increase the risk of infection.^{5,6} In addition, they require a complex tapering schedule and rebound inflammation. Currently, there is a growing interest in seeking alternative drugs such as nonsteroidal anti-inflammatory drugs (NSAIDs).^[5] They have advantages such as stable IOP, lower risk of infection, and the additional benefit of analgesia. The use of NSAIDs in uneventful phacoemulsification without any high-risk factors is still controversial.

Previous studies suggest NSAIDs to be more or equally effective than steroids and their synergistic effect to control inflammation.^[1,5,7-17] However, the literature comparing the efficacy of NSAIDs (particularly nepafenac 0.3%) with prednisolone acetate 1% is still lacking.^[11,15-17]

Thus, we compared the safety and efficacy of various NSAIDs with prednisolone acetate after uneventful phacoemulsification.

Material and methods

This prospective, comparative study conducted in the Department of Ophthalmology, Patna Medical College and Hospital, Patna, Bihar, India, for 12 months. This study comparing nepafenac (0.1%), bromfenac (0.07%), preservative-

free ketorolac (0.4%), nepafenac (0.3%), and prednisolone acetate (1%) eye drops in patients undergoing uncomplicated phacoemulsification. The local ethics committee approved the study protocol. The trial was conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent is routinely obtained from all patients undergoing cataract surgery.

Methodology

All patients undergoing uneventful phacoemulsification with in the bag IOL were included. Patients were randomly assigned to receive any one of the five anti-inflammatory drugs with one drug assigned on each operation day randomly. These were topical nepafenac (0.1%), bromfenac (0.07%), ketorolac (0.4%), nepafenac (0.3%), or prednisolone (1%). The exclusion criteria were presence of chronic ocular inflammation, presence of any other ocular pathology, history of use of topical NSAIDs or steroids or oral alpha agonists such as tamsulosin or oral or inhalational steroids or NSAIDs, history of previous ocular trauma or surgery, diabetics who had retinopathy, presence of any intra or postoperative complication, any cause of poor vision after surgery other than CME, noncompliance with follow-ups, any known hypersensitivity to the drugs administered, and any eye with poorly dilating pupil or which required any pupil expansion device. All grades of cataract were included in the study; however, to avoid bias, we excluded eyes where the cumulative dissipated energy was more than 20 and those with any intraoperative complication.

All patients received topical therapy including Moxifloxacin hydrochloride 0.5% four times a day, the anti-inflammatory drug, and carboxymethyl cellulose 1% four times a day. All patients underwent a suture less 2.2-mm clear cornea incision, continuous curvilinear

capsulorhexis, phacoemulsification using the direct chop technique with Centurion Vision System, and implantation of hydrophobic acrylic foldable IOL in bag. All surgical procedures used balanced salt solution (BSS, Alcon Laboratories, Inc.) and 1.4% hyaluronic cohesive viscoelastic (Aurogel 1.4% w/v, Aurolab, Tamil Nadu, India). All patients were operated and followed postoperatively by a single surgeon (AN).

Patients were divided into five groups based on the anti-inflammatory treatment used before the surgery on the same day. The treatment regimen used in all the groups is as follows:

- Group 1: prednisolone acetate 1% [n = 91] six times a day, tapered weekly for 6 weeks
- Group 2: bromfenac (0.07%) [n = 93] twice daily for 6 weeks
- Group 3: preservative-free Ketorolac (0.45%) [n = 94] twice daily for 6 weeks
- Group 4: nepafenac (0.1%) [n = 96] thrice daily for 6 weeks
- Group 5: nepafenac (0.3%) [n = 96] once daily for 6 weeks.

Data from all patients were analyzed at baseline and at 1 and 6 weeks after surgery. Signs of postoperative inflammation were evaluated. Compliance with medications was assessed by asking the patients whether they have used all medicines as advised during their follow-up visits. Ocular pain was graded using a category scale where 0 indicates no pain, 1 indicates occasional pain, 2 indicates mild pain occurring almost daily but not significant enough to take oral medication, and 3 indicates moderate to severe pain requiring an oral analgesic. Slit-lamp assessment was performed for the following signs: (1) conjunctival hyperemia, which was graded as per the International Chronic Ocular Graft vs Host Disease (GVHD) Consensus Group [grade

0 = none, grade 1 = mild/moderate, and grade 2 = severe]; (2) cells in the anterior chamber (AC), which were graded from 0 to 4 as per the standardization of uveitis nomenclature (SUN) classification of severity of uveitis.[18,19]

The visual acuity recorded using Snellen's chart was converted into logMAR and analyzed at each visit. Best-corrected visual acuity (BCVA) less than 6/9 at last follow-up was considered as poor outcome.

Post-operatively, macular thickening or CME was assessed using a swept-source optical coherence tomography (OCT) device [DRI Triton Topcon, SS-OCT. A single experienced ophthalmic technician performed all the scans at baseline, 7 days, and 6 weeks post-surgery. Central macular thickness (CMT) was obtained using 6-mm cube scan centered on the fovea. Increase in CMT is an objective indicator of macular swelling and can be used to demonstrate the amount of inflammation after cataract surgery. As it has been reported that an average increase in foveal thickness of 10–22 (+/- 24) microns occurs after an uncomplicated phacoemulsification, an increase in CMT by 40 microns or more on OCT was considered to be significant and taken as a criterion for analysis.[20] Clinical CME was defined as a significant increase in CMT along with visible cystic changes and final BCVA less than 6/9. Intraocular pressure (IOP) was measured using a noncontact pneumo-tonometer at all visits. The primary outcome was intraocular inflammation evaluated by AC cells at 1 and 6 weeks after surgery. Secondary outcomes included conjunctival hyperemia, corneal edema, BCVA, and CMT on OCT at 1 and 6 weeks after surgery.

Results

A total of 500 patients were assessed and randomized into five groups (100 in each group). Out of these, 30 eyes were excluded due to more than 20 CDE or any intraoperative complication. Thus, 470 patients met the inclusion criteria and were included for analysis. Baseline characteristics were assessed before the surgery and after randomization into the groups. These are mentioned in Table 1. There was no significant difference in the baseline characters (age, gender distribution, and baseline BCVA) among any groups.

Anterior chamber (AC) cells

Evaluation of AC cells at 1 week showed that 35%–60% of patients had no AC cells (grade 0) [Table 2]. There was no significant difference in the percentage of patients with AC cells grade of 0, 1+, and 2+ between the steroid group (group 1) and NSAIDs groups at 1-week follow-up [Table 2]. However, the number of patients with grade 0 AC cells was maximum in the nepafenac 0.3% group (58/96, 60.4%) and least in the bromfenac 0.07% group (33/93, 35.5%) at 1-week follow-up. None of the patients had cells at 6-week follow-up. Thus, the bromfenac group showed the least potency and the nepafenac 0.3% group showed maximal potency in control of AC inflammation though not statistically significant.

Ocular pain score

Analysis of pain score at 1 week showed that more than 90% of patients in each group had no pain [Table 2]. There was no significant difference in the percentage of patients with a pain score of 0 and 1 between the steroid group (group 1) and NSAIDs groups at 1 week. However, the number of patients with a pain score of 0 was maximum in the nepafenac 0.3% group, which was similar to that in the prednisolone group at 1-week follow-up.

Patients in all groups achieved a pain score of 0 at 6-week follow-up.

Conjunctival hyperemia or congestion

Analysis of congestion score at 1 week showed that 62%–81% of patients had no congestion [Table 2]. There was no significant difference in the percentage of patients with a congestion score of 1 between the steroid group (group 1) and ketorolac, nepafenac 0.1%, and nepafenac 0.3% groups at 1-week follow-up, with the least number of patients in the nepafenac 0.3% group. However, the number of patients with a congestion score of 1 was significantly more in the bromfenac 0.07% group as compared to the prednisolone group at 1-week follow-up ($P = 0.04$). Patients in all groups achieved a congestion score of 0 at 6-week follow-up. All NSAIDs were comparable to prednisolone in reducing conjunctival congestion except bromfenac that was the least effective.

Central macular thickness

Central macular thickness (CMT) was compared in all the groups [Table 3]. At 1 week, although none of the cases had any cystic spaces evident in OCT, few patients had an increase in CMT by more than 40 microns [Table 3]. On comparison of prednisolone and NSAIDs, the percentage of patients with more than 40 microns increase in CMT was significantly higher in the bromfenac group ($P = 0.003$) and in the nepafenac 0.1% group ($P = 0.03$). None of the patients in the nepafenac 0.3% group and only 1 patient in the prednisolone group developed a significant increase in CMT. Thus, in comparison to prednisolone, bromfenac and nepafenac 0.1% are less effective in preventing an increase in CMT.

However, by 6 weeks, there was no significant difference in the number of patients with a significant increase in CMT between the steroid with NSAID groups.

Bromfenac proved to be the least efficacious in preventing macular edema with the maximum percentage of patients with an increase of CMT by more than 40 microns (15.1%) at 6 weeks. Similarly, the percentage of patients with clinical CME was least in the nepafenac 0.1% (1%) and 0.3% (1%) groups but highest in the prednisolone group (4.3%) at 6 weeks though not statistically significant ($P = 0.34$).

The mean (SD) of the change in CMT from baseline to 1-week postoperative period was compared between prednisolone and NSAIDs groups. It was found that there was an increase in CMT at

1 week in all groups, which was minimum in the nepafenac 0.3% group. On comparison with prednisolone, there was a significantly lower increase in CMT in the nepafenac 0.3% group ($P = 0.003$) but a significantly higher increase in CMT in the ketorolac and bromfenac group ($P = 0.006$ and 0.004 , respectively).

At 6 weeks, the mean increase in CMT from baseline was similar between the prednisolone group and NSAIDs group except in the nepafenac 0.3% group that showed less increase in CMT as compared to prednisolone ($P = 0.004$). Thus, nepafenac 0.3% might be more effective than prednisolone in preventing CME.

Table 1: Baseline characteristics among all groups

Parameter	Prednisolone	Bromfenac	Ketorolac	Nepafenac	Nepafenac
	1% group 1	0.07% group	0.4% group	0.1% group	0.3% group
	(n=91)	2 (n=93)	3 (n=94)	4 (n=96)	5 (n=96)
Age (years) Mean (SD)	65.4 (9.0)	62.6 (13.1)	62.9 (11.3)	65.9 (8.5)	64 (6.6)
<i>P</i> -value (comparing with prednisolone)		0.29	0.24	0.43	0.42
Male: Female (n)	60:31	50:43	51:43	58:38	52:44
<i>P</i> -value (comparing with prednisolone)		0.09	0.10	0.43	0.10
DM (n)	35 (38.5%)	28 (30.1%)	28 (29.8%)	27 (28.1%)	28 (29.2%)
<i>P</i> -value (comparing with prednisolone)		0.23	0.21	0.13	0.18
Mean BCVA pre-op (logMAR)	0.93 (0.58)	1.05 (0.65)	1.05 (0.58)	1.20 (0.66)	0.82 (0.46)
<i>P</i> -value (comparing with prednisolone)		0.23	0.06	0.06	0.42

Table 2: Comparison of AC cells, ocular pain and conjunctival congestion score among all groups

Inflammation Sign	Score	Prednisolone	Bromfenac	Ketorolac	Nepafenac	Nepafenac
		1% group 1	0.07% group	0.4% group	0.1% group	0.3% group
		(n=91)	2 (n=93)	3 (n=94)	4 (n=96)	5 (n=96)
Cells in AC 1 week	0 n (%)	48 (52.7%)	33 (35.5%)	53 (56.4%)	51 (53.1%)	58 (60.4%)
	1 n (%)	42 (46.2%)	58 (62.4%)	40 (42.6%)	42 (43.8%)	36 (37.5%)
	2 or more n (%)	1 (1.1%)	2 (2.2%)	1 (1.1%)	3 (3.1%)	2 (2.1%)
<i>P</i> (comparing with prednisolone)			0.05	0.88	0.61	0.44
Cell in AC 6 weeks	0 n (%)	91 (100%)	93 (100%)	94 (100%)	96 (100%)	96 (100%)
Pain score 1	0 n (%)	87 (95.6%)	87 (93.5%)	85 (90.4%)	88 (91.7%)	92

week						(95.8%)
	1 n (%)	4 (4.4%)	6 (6.5%)	9 (9.6%)	8 (8.3%)	4 (4.2%)
	<i>P-value</i> (comparison with prednisolone)		0.539	0.168	0.272	0.938
Pain score 6 week	0 n (%)	91 (100%)	93 (100%)	94 (100%)	96 (100%)	96 (100%)
Congestion 1 week	0 n (%)	69 (75.8%)	58 (62.4%)	76 (80.9%)	61 (63.5%)	78 (81.3%)
	1 n (%)	22 (24.2%)	35 (37.6%)	18 (19.1%)	34 (35.4%)	16 (16.7%)
	2 n (%)	0 (0%)	0 (0%)	0 (0%)	1 (1%)	2 (2.1%)
<i>P-value</i> (comparing with prednisolone)			0.04	0.40	0.05	0.18
Congestion 6 weeks	0 n (%)	91 (100%)	93 (100%)	94 (100%)	96 (100%)	96 (100%)

Table 3: Comparison of change in CMT from baseline among different groups

Time	Parameter	Prednisolone	Bromfenac	Ketorolac	Nepafenac	Nepafenac
(1 week-Base line)	n (%) of patients with increase in CMT >40 microns	1 (1.1%)	11 (11.8%)	4 (4.3%)	7 (7.3%)	0 (0%)
<i>P-value</i> (Comparison with prednisolone)			0.003	0.18	0.03	0.30
(6 week-baseline)	n (%) of patients with increase in CMT >40 microns	6 (6.6%)	14 (15.1%)	3 (3.2%)	8 (8.3%)	3 (3.1%)
<i>P-value</i> (Comparison with prednisolone)			0.06	0.28	0.65	0.26
(6 week-baseline)	n (%) of patients with clinical CME	4 (4.3%)	3 (3.2%)	2 (2.1%)	1 (1.0%)	1 (1.0%)
<i>P-value</i> (Comparison with prednisolone)			0.51	1.0	0.34	0.34
(1 week-Base line)	Change in the CMT from baseline Mean (SD)	5.1 (14.9)	14.5 (24.4)	11.5 (16.5)	2.8 (23.3)	1.1 (16.0)
<i>P-value</i> (Comparison with prednisolone)			0.006	0.004	0.38	0.003
(6 week-baseline)	Change in the CMT from baseline Mean (SD)	13.6 (21.0)	21.4 (30.2)	15.4 (15.2)	12.0 (22.7)	6.8 (11.6)
<i>P-value</i> (Comparison with prednisolone)			0.05	0.06	0.59	0.004

Table 4: Comparison of visual outcome among all groups

Parameter	Time of evaluation	Prednisolone 1% group 1 (n=91)	Bromfenac 0.07% group 2 (n=93)	Ketorolac 0.4% group 3 (n=94)	Nepafenac 0.1% group 4 (n=96)	Nepafenac 0.3% group 5 (n=96)
BCVA mean (SD)	Baseline	0.93 (0.58)	1.05 (0.65)	1.05 (0.58)	1.20 (0.66)	0.82 (0.46)
<i>P</i> (comparing with prednisolone)			0.239	0.06	0.05	0.42
BCVA mean (SD)	6 weeks	0.08 (0.13)	0.07 (0.10)	0.08 (0.14)	0.07 (0.11)	0.07 (0.08)

<i>P</i> (comparing with prednisolone)			0.89	0.94	0.93	0.35
<i>n</i> (%) patients	Baseline	0 (0%)	1 (1.1%)	0 (0%)	4 (4.2%)	6 (6.3%)
with BCVA	<i>P</i> (comparing with prednisolone)		0.321	0.95	0.05	0.01
6/9 or better	6 weeks	84 (92.3%)	89 (95.7%)	89 (94.7%)	90 (93.8%)	93 (96.9%)
<i>P</i> (comparing with prednisolone)			0.332	0.512	0.698	0.165

The mean (SD) of baseline BCVA and at 6-week follow-up was statistically similar between steroid and NSAID groups [Table 4]. The percentage of patients with BCVA better than or equal to 6/9 at 6-week follow-up was statistically similar among all groups [Table 5].

All NSAID preparations were well tolerated; among them, ketorolac group had some patients (3/94, 3.1%) with mild to moderate discomfort at 1 week. IOP was within the normal range in all except 1 out of 91 (1.0%) in the steroid group who needed anti-glaucoma medication.

Discussion

Corticosteroids act much higher in the inflammatory cascade by inhibiting phospholipase-A2 and preventing the formation of arachidonic acid (AA). They also inhibit lipo-oxygenase (LOX) pathway in addition to cyclooxygenase (COX). AA is metabolized to leukotrienes and prostaglandins, which mediate the inflammatory response. Corticosteroids also down regulate genes that encode cytokines, chemokines, adhesion molecules, inflammatory enzymes, receptors, and proteins.[21] NSAIDs prevent the conversion of AA to prostacyclins, thromboxanes, and prostaglandins by inhibiting COX. As steroids have a broader anti-inflammatory action, theoretically it seems that steroids should be more effective in treating post-surgery inflammation and preventing CME.

The major drawbacks of steroids include raised IOP, delayed wound healing, increased risk of infection, and complex tapering regimen. Due to these drawbacks, NSAIDs have been explored to reduce inflammation.[1,7-14,21,22] However, NSAIDs have been reported to be more effective in re-establishing the blood-aqueous barrier as measured by anterior ocular fluorophotometry.[5]

The literature comparing the efficacy of all available NSAIDs with the most effective steroid that is prednisolone acetate is still lacking.[11,15-17] We compared the safety and efficacy of various available topical NSAIDs with prednisolone acetate in controlling inflammation.

Malik et al.[17] compared topical prednisolone 1% and nepafenac 0.1%, bromfenac 0.09%, and ketorolac 0.5% in patients with uneventful phacoemulsification in a prospective randomized study involving 200 patients. They reported that prednisolone was most effective to control AC cells and flare, whereas nepafenac was most effective among NSAIDs to control AC flare at the 2nd week. Demco et al.[23] reported that diclofenac 0.01% was as effective, safe, and well-tolerated as prednisolone acetate 1.0%. Similar results were obtained by el-Harazi et al.¹¹ In our study, the percentage of patients with cells grade 0, 1+, and 2+ was found to be statistically similar in all groups at 1 week; the lowest percentage was found in nepafenac 0.3%. Thus, NSAIDs, particularly nepafenac 0.3% and ketorolac 0.45%, can be considered to be as effective as prednisolone in controlling postoperative inflammation.

The beneficial effect of NSAIDs over steroids in previous literature can be explained by the use of steroids such as dexamethasone, betamethasone, and fluorometholone in most of the comparative studies.[13,21,22,24,25] These steroids, though more potent than prednisolone acetate, are known to have a lower intraocular penetration, which leads to an overall less efficacy than prednisolone acetate.[16,26]

Kessel et al.[9] performed a systematic review to compare the efficacy of NSAIDs (diclofenac, nepafenac, ketorolac, and bromfenac) versus steroids (dexamethasone, betamethasone, and fluorometholone). They concluded that topical NSAIDs are more effective than steroids in preventing inflammation and reducing the prevalence of CME after uncomplicated phacoemulsification. Thus, our study comparing NSAIDs including nepafenac 0.3% with prednisolone acetate 1% might be an important addition.

Juthani et al.[21] performed a Cochrane review comparing NSAIDs (alone or in combination with topical steroids) versus topical steroids and concluded that there was insufficient evidence to prove equivalence or superiority of NSAIDs or combination over steroids alone. However, the risk of CME may be lower with NSAIDs or combination than steroids alone.

Our study evaluated all outcomes in terms of percentage or proportion of patients and compared all parameters of intraocular inflammation between the groups. In our study, there was no significant difference between the prednisolone and NSAIDs groups with regard to ocular pain and conjunctival hyperemia; however, nepafenac 0.3% was found to be most effective.

Malik et al.[17] reported that ketorolac 0.5% and nepafenac 0.1% were equally effective in controlling postoperative

ocular pain and hyperemia, whereas prednisolone is best for inflammation control. These differences between our study and Malik et al.[17] can be attributed to the inclusion of nepafenac 0.3% in ours, which was not included in their study. This shows that nepafenac 0.3% might be most effective to control pain, inflammation, and hyperemia when compared with other NSAIDs and prednisolone.

Better efficacy of nepafenac can be explained by the following reasons. It can achieve up to 96% inhibition of PGE₂ in vitreous and aqueous humor versus <1% with diclofenac and 8% with ketorolac, as demonstrated in an animal study.[5] In our study, prednisolone and nepafenac 0.3% were found to be more effective in preventing the increase of CMT as compared to other NSAIDs and the difference was statistically significant at 1 week. Bromfenac and nepafenac 0.1% were the least effective. However, at 6 weeks, nepafenac 0.3% showed a minimum increase in CFT ($P = 0.004$) whereas other NSAIDs and prednisolone were comparable. Similarly, the percentage of patients with clinical CME was lowest in nepafenac 0.1 and 0.3% groups ($P = 0.34$).

Previous studies suggest that topical NSAIDs, particularly bromfenac 0.09% and combination therapy, are more or equally effective than topical steroids alone in preventing CME.[9,10,13,21,25,27] However, none has compared the incidence of CME including nepafenac 0.3% and prednisolone acetate. Visual outcome and change in IOP were found to be comparable among all groups at 6 weeks.

NSAIDs can cause ocular surface toxicity such as transient burning, stinging, conjunctival hyperemia, superficial punctate keratitis, corneal infiltrates and epithelial defects, and stromal melt.[5] However, these are rare and often accompany inappropriate and prolonged

use of NSAIDs.^[28] In our group of patients, NSAIDs were well tolerated except the ketorolac group, which had 3.1% of patients with mild discomfort and burning sensation.

The major strength of our study is that this is the first study comparing the efficacy of nepafenac 0.3% with the most potent steroid prednisolone acetate 1% post phacoemulsification. Nepafenac 0.3% was found to be more effective than prednisolone in preventing subclinical and clinical CME.^[29,30] This can help to limit the use of steroids in post-cataract surgery patients, thereby avoiding the drawbacks of topical steroids. All other NSAIDs were found to be comparable to prednisolone in controlling postoperative inflammation.

Conclusion

We recommend that nepafenac 0.3% can be used as a sole anti-inflammatory agent in patients with uneventful phacoemulsification and combination therapy can be used in high-risk cases.

References

1. Kim SJ, Schoenberger SD, Thorne JE, Ehlers JP, Yeh S, Bakri SJ. Topical nonsteroidal anti-inflammatory drugs and cataract surgery: A report by the American Academy of Ophthalmology. *Ophthalmology* 2015;122:2159–68.
2. Lobo CL, Faria PM, Soares MA, Bernardes RC, Cunha-Vaz JG. Macular alterations after small-incision cataract surgery. *J Cataract Refract Surg* 2004;30:752–60.
3. McCafferty S, Harris A, Kew C, Kassam T, Lane L, Levine J, *et al.* Pseudophakic cystoid macular edema prevention and risk factors; prospective study with adjunctive once daily topical nepafenac 0.3% versus placebo. *BMC Ophthalmol* 2017;17:16.
4. Montes J, Erakgun T, Afrashi F, Kerci G. Incidence of cystoid macular edema after uncomplicated phacoemulsification. *Ophthalmologica* 2003;217:408–12.
5. O'Brien TP. Emerging guidelines for use of NSAID therapy to optimize cataract surgery patient care. *Curr Med Res Opin* 2005;21:1131–7.
6. Heier JS, Topping TM, Baumann W, Dirks MS, Chern S. Ketorolac versus prednisolone versus combination therapy in the treatment of acute pseudophakic cystoid macular edema. *Ophthalmology* 2000;107:2034–8;discussion 2039.
7. Pal DN, Subramanian DT, Bosco DAJ, Chawda DV. Comparative study of the effect of topical corticosteroid with non-steroidal anti inflammatory agents on post-operative inflammation and corneal astigmatism after cataract surgery. *J Curr Med Res Opin* 2019;2:95–9.
8. Zhao X, Xia S, Wang E, Chen Y. Comparison of the efficacy and patients' tolerability of Nepafenac and Ketorolac in the treatment of ocular inflammation following cataract surgery: A meta-analysis of randomized controlled trials. *PloS One* 2017;12:e0173254.
9. Kessel L, Tendal B, Jørgensen KJ, Erngaard D, Flesner P, Andresen JL, *et al.* Post-cataract prevention of inflammation and macular edema by steroid and nonsteroidal anti-inflammatory eye drops: A systematic review. *Ophthalmology* 2014;121:1915–24.
10. Coassin M, De Maria M, Mastrofilippo V, Braglia L, Cimino L, Sartori A, *et al.* Anterior chamber inflammation after cataract surgery: A randomized clinical trial comparing bromfenac 0.09% to dexamethasone 0.1. *Adv Ther* 2019;36:2712–22.

11. el-Harazi SM, Ruiz RS, Feldman RM, Villanueva G, Chuang AZ. A randomized double-masked trial comparing ketorolac tromethamine 0.5%, diclofenac sodium 0.1%, and prednisolone acetate 1% in reducing post-phacoemulsification flare and cells. *Ophthalmic Surg Lasers* 1998;29:539–44.
12. Ylinen P, Taipale C, Lindholm J-M, Laine I, Holmström E, Tuuminen R. Postoperative management in cataract surgery: nepafenac and preservative-free diclofenac compared. *Acta Ophthalmol (Copenh)* 2018;96:853–9.
13. Walter K, Kauffman L, Hess J. Rate of pseudophakic cystoid macular edema using intraoperative and topical nonsteroidal antiinflammatory drugs alone without steroids. *J Cataract Refract Surg* 2020;46:350–4.
14. Walter KA, Lee RY, Chen K, Komanski C. Incidence of cystoid macular edema following routine cataract surgery using NSAIDs alone or with corticosteroids. *Arq Bras Oftalmol* 2020;83:55–61.
15. Kupferman A, Leibowitz HM. Anti-inflammatory effectiveness of topically administered corticosteroids in the cornea without epithelium. *Invest Ophthalmol* 1975;14:252–5.
16. McGhee CN, Watson DG, Midgley JM, Noble MJ, Dutton GN, Fern AI. Penetration of synthetic corticosteroids into human aqueous humour. *Eye (Lond)* 1990;4:526–30.
17. Malik A, Sadafale A, Gupta YK, Gupta A. A comparative study of various topical nonsteroidal anti-inflammatory drugs to steroid drops for control of post cataract surgery inflammation. *Oman J Ophthalmol* 2016;9:150–6.
18. Manfred, D. . (2022). May There Exist Healthy Diseases?. *Journal of Medical Research and Health Sciences*, 5(3), 1801–1803.
19. Ogawa Y, Kim SK, Dana R, Clayton J, Jain S, Rosenblatt MI, *et al.* International Chronic Ocular Graft-vs-Host-Disease (GVHD) Consensus Group: proposed diagnostic criteria for chronic GVHD (Part I). *Sci Rep* 2013;3:3419.
20. 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.
21. Pardianto G, Moeloek N, Reveny J, Wage S, Satari I, Sembiring R, *et al.* Retinal thickness changes after phacoemulsification. *Clin Ophthalmol Auckl NZ* 2013;7:2207–14.
22. Juthani VV, Clearfield E, Chuck RS. Non-steroidal anti-inflammatory drugs versus corticosteroids for controlling inflammation after uncomplicated cataract surgery. *Cochrane Database Syst Rev* 2017;7:CD010516.
23. Sheppard JD. Topical bromfenac for prevention and treatment of cystoid macular edema following cataract surgery: A review. *Clin Ophthalmol Auckl NZ* 2016;10:2099–111.
24. Demco TA, Sutton H, Demco CJ, Raj PS. Topical diclofenac sodium compared with prednisolone acetate after phacoemulsification-lens implant surgery. *Eur J Ophthalmol* 1997;7:236–40.
25. Myers WG. Interpretation of ESCRS PREMEDI study report 1. *J Cataract Refract Surg* 2019;45:114–5.
26. Wielders LHP, Schouten JSAG, Nuijts RMMA. Prevention of macular edema after cataract surgery. *Curr Opin Ophthalmol* 2018;29:48–53.
27. Diestelhorst M, Aspacher F, Konen W, Kriegelstein GK, Hilgers RD. Effect of dexamethasone 0.1% and prednisolone

- acetate 1.0% eye drops on the blood-aqueous barrier after cataract surgery: A controlled randomized fluorophotometric study. *Graefes Arch Clin Exp Ophthalmol Albrecht Von Graefes Arch Klin Exp Ophthalmol* 1992;230:451–3.
28. Cardascia N, Palmisano C, Centoducati T, Alessio G. Topical nonsteroidal anti-inflammatory drugs as adjuvant therapy in the prevention of macular edema after cataract surgery. *Int Ophthalmol* 2017;37:1127–31.
29. Kim SJ, Flach AJ, Jampol LM. Nonsteroidal anti-inflammatory drugs in ophthalmology. *Surv Ophthalmol* 2010;55:108–33.
30. Sahu S, Ram J, Bansal R, Pandav SS, Gupta A. 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.