Comparison of Nepafenac 0.1% Versus Prednisolone Acetate 1% Ophthalmic Suspensions Regarding the Effect on Ocular Inflammation and Central Macular Thickness After Uneventful Phacoemulsification

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Abstract

Background: **Cataract surgery triggers an inflammatory reaction that, if unmanaged, can lead to significant postoperative complications.** ***Aim:*** **This study aimed to evaluate and compare the effects of nepafenac 0.1% and prednisolone acetate 1% eye drops on ocular inflammation and central macular thickness following cataract surgery.** ***Subjects and methods:*** **A randomized clinical trial was performed involving patients who underwent phacoemulsification at Suez Canal University Hospital. Patients were allocated through randomization into two groups: Group A administered nepafenac 0.1% and Group B received prednisolone acetate 1%. All patients were scheduled for follow-up on days 1, 4, 7, and 30 after surgery, where visual acuity (VA); Intraocular pressure (IOP), and ocular inflammation were evaluated. CMT was assessed on days 7 and 30.** ***Results:*** **Postoperative visual acuity, intraocular pressure, and ocular inflammation did not differ significantly between the two groups. A significant difference between the groups was detected in ocular discomfort, photophobia, and central corneal thickness (CCT) on postoperative day 7; where for nepafenac and prednisolone mean ± SD of ocular discomfort was 1.20 ± 0.41 and 1.68 ± 0.75, respectively(P=0.007) and for CCT was 543.40 ± 42.13 and 580.36 ± 52.02, respectively(P=0.008). At postoperative day 30, the two groups showed a statistically significant difference in the change in central macular thickness relative to baseline values, where the mean was 3.68 ± 33.96 and 26.0 ± 28.14 for nepafenac and prednisolone, respectively (P=0.017).** ***Conclusion:*** **Topical nepafenac 0.1% may serve as an effective and safer alternative to corticosteroids for controlling postoperative inflammation following cataract surgery.**

Keywords: Cataract surgery; Eye inflammation; CMT; Anti-inflammatory eye drops.

Introduction

Cataract continues to be the primary cause of reversible blindness globally [(1)]. Cataract extraction is among the most frequently performed surgical procedures globally [(2)]. Postoperative anterior segment inflammation is one of the most common complications following phacoemulsification [(3)]. If inadequately controlled, ocular inflammation may persist, leading to patient discomfort, pain, corneal edema, intraocular pressure (IOP) elevation, cystoid macular edema (CME), and posterior capsule opacification[(4)].

Pseudophakic cystoid macular edema (PCME) is a recognized and well-documented postoperative complication [(5)]. that typically develops within 4 to 12 weeks after surgery [(6)]. Although topical corticosteroids remain the mainstay for controlling postoperative inflammation [(7)], prolonged use can result in adverse effects such as elevated IOP, delayed wound healing, and increased susceptibility to

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infection [8]. Patients who exhibit an IOP rise in response to corticosteroid use are described as "steroid responders" [9].

Nonsteroidal anti-inflammatory drugs (NSAIDs) provide comparable anti-inflammatory efficacy to corticosteroids in uncomplicated cataract surgery, with a lower risk of these side effects [10]. Commonly used topical NSAIDs include ketorolac tromethamine, diclofenac, flurbiprofen, indomethacin, bromfenac, and nepafenac [11]. Nepafenac is a prodrug converted by intraocular hydrolases to amfenac, which exhibits superior penetration into both the anterior and posterior segments following topical administration [11].

This study aimed to compare the efficacy of nepafenac 0.1% and prednisolone acetate 1% ophthalmic suspensions in controlling postoperative ocular inflammation and central macular thickness, to optimize visual outcomes and patient comfort after cataract surgery.

Subjects And Methods

Study design and setting

A randomized clinical trial was conducted at Suez Canal University Hospital on patients scheduled to undergo phacoemulsification. The study period extended from April 2022 to December 2022.

Study population and randomization

Eligible participants were assigned to one of two treatment arms through randomization. Participants in Group A were administered topical nepafenac 0.1% four times daily for a duration of four weeks postoperatively. Group B received topical prednisolone acetate 1%, also four times daily, with the dosage gradually tapered by one drop per week over the same four-week period. Participants were assigned randomly through a sequence generated by computer to ensure that baseline characteristics were comparable between the groups. To preserve allocation concealment, an independent researcher who was not involved in patient enrollment or outcome assessment created sequentially numbered sealed envelopes.

Inclusion and exclusion criteria

Participants were 50 years of age or older, including both males and females, and diagnosed with senile cataract. Patients with a history of glaucoma or retinal disease, intraocular inflammation, or previous ocular surgeries such as vitrectomy or keratoplasty were excluded. Additional exclusion criteria included the presence of dense cataracts that precluded macular OCT imaging, and any known hypersensitivity or allergic reaction to NSAIDs or any study medication component.

Sample size

The required sample size was determined using a two-sample t-test, aiming to detect a mean difference of 20 μm in postoperative central macular thickness between the two treatment groups. Calculations assumed a standard deviation of 25 μm, a significance level (α) of 0.05, and 80% statistical power ($\beta = 0.20$). Based on these assumptions, approximately 25 eyes per group were needed, resulting in a total of 50 eyes for the study.

Data collection and preoperative evaluation

Each participant completed a standardized history-taking sheet, and all underwent comprehensive ophthalmic examinations. All participants completed a standardized history form and underwent a thorough ophthalmic evaluation. Preoperative assessments comprised best-corrected

visual acuity (BCVA), slit-lamp biomicroscopy, fundus examination, and intraocular pressure (IOP) measurement using a Goldmann applanation tonometer. Imaging evaluations included swept-source optical coherence tomography (OCT) for central macular thickness (CMT) assessment and specular microscopy to determine central corneal thickness (CCT).

Surgical Procedure and Postoperative Management

All surgeries were performed under topical anesthesia by a single experienced consultant ophthalmologist to ensure consistency. A standardized phacoemulsification technique was used in all cases. After proper aseptic preparation and draping, a sterile eyelid speculum was inserted. A side-port incision was first created at the corneal periphery, followed by a 2.8 mm clear corneal main incision using a keratome.

Methylcellulose 2% (preservative-free) was instilled into the anterior chamber as the viscoelastic substance preserves anterior chamber stability and safeguard the corneal endothelial cells. A bent cystotome needle was then used to construct a continuous curvilinear capsulorhexis with a diameter of roughly 5.0 to 5.5 mm while being shielded by viscoelastic material. Hydrodissection and hydrodelineation were carried out with balanced salt solution to ensure adequate nucleus mobility. Phacoemulsification was performed using the Signature® phacoemulsification system (Abbott Medical Optics, USA) with the stop-and-chop technique. Nucleus fragments were emulsified and aspirated, followed by irrigation and aspiration of residual cortical material.

The capsular bag was refilled with methylcellulose, and an AcrySof® hydrophobic acrylic intraocular lens (Alcon Laboratories, USA) was carefully inserted into the capsular bag using a single-use injector. The viscoelastic material was completely removed by irrigation and aspiration, and the incisions were hydrated with balanced salt solution to ensure watertight closure. No sutures were required in any case.

At the end of surgery, topical tobramycin/dexamethasone ointment was applied, and an eye shield was placed for overnight protection.

Postoperative regimen:

All patients received topical tobramycin/dexamethasone eye ointment for one week postoperatively and systemic moxifloxacin 400 mg once daily for three days. Topical tobramycin/dexamethasone eye ointment continued for one week. According to group allocation:

- Group A was given nepafenac 0.1% ophthalmic suspension four times daily for four weeks.
- Group B received prednisolone acetate 1% eye drops four times each day, tapered every week for four weeks.

Follow-up and outcome assessment:

Patients were examined on postoperative days 1, 4, 7, and 30. Follow-up evaluations included BCVA, IOP measurement, and assessment of ocular inflammation. The anterior chamber (AC) cells and flare were rated using the Standardization of Uveitis Nomenclature (SUN) standards [12]. Conjunctival hyperemia was evaluated using the International Chronic Ocular Graft-versus-Host Disease (GVHD) Consensus Group grading system[13]. Ocular pain and discomfort were graded using a categorical scale[14]. Corneal edema, ocular discomfort, and photophobia were also recorded. Central macular thickness

(CMT) was re-evaluated using OCT at postoperative days 7 and 30.

The study was conducted in a single-blind manner. Although the two study medications had different packaging, the examiner responsible for postoperative evaluation including anterior chamber inflammation grading, IOP measurement, and OCT imaging was blinded to group allocation to minimize observer bias.

Statistical analysis

IBM SPSS Statistics version 20.0 (IBM Corp., Chicago, IL, USA) was used to process the data after it had been entered and coded in Microsoft Excel 2010. While continuous data were presented as means ± standard deviation (SD), categorical variables were presented as frequencies and percentages. The Chi-square or Fisher's exact test was implemented for qualitative comparisons, while the independent-samples t-test or Mann-Whitney U test was deployed for quantitative data as appropriate. To compare groups within themselves, the paired-samples t-test was employed. The normality of the data was evaluated using the Shapiro-Wilk test; a p-value < 0.05 denotes statistical significance.

Results

Our study demonstrated that, regarding best-corrected visual acuity (BCVA) in LogMAR notation, a significant difference between the two groups was detected on postoperative days 1 and 4. **(Table 1)**. The mean postoperative BCVA on day 1 was 0.56 ± 0.24 in Group A and 0.84 ± 0.46 in Group B (p = 0.002). On postoperative day 4, the mean BCVA values were 0.32 ± 0.16 in Group A and 0.51 ± 0.35 in Group B (p = 0.014). By postoperative days 7 and 30, however, no statistically significant difference was detected between the two study groups.

In terms of intraocular pressure (IOP), a statistically significant difference was found only on postoperative day 1, where the mean IOP was 12.32 ± 1.89 mmHg in Group A and 12.96 ± 1.31 mmHg in Group B (p = 0.027). On postoperative days 4, 7, and 30, no statistically significant difference in IOP was observed between the two groups.

As presented in Table (1), evaluation of ocular inflammation parameters including anterior chamber (AC) cells, AC flare, conjunctival hyperemia, and ocular pain revealed no statistically significant difference between the two groups at any postoperative visit. However, regarding ocular discomfort and photophobia, a statistically significant difference was observed on postoperative day 7 (p = 0.003), with patients in Group A showing lower symptom severity compared to Group B. On postoperative days 1, 4, and 30, no significant differences were found between the groups for these symptoms.

For corneal edema, a statistically significant difference was identified between the two study groups on postoperative days 4 and 7 **(Table 1)**. The mean central corneal thickness (CCT) in Group A and Group B at postoperative day 4 was 547.52 ± 42.19 µm and 602.48 ± 98.63 µm, respectively (p = 0.014), while at postoperative day 7 the mean values were 543.40 ± 42.13 µm and 580.36 ± 52.02 µm, respectively (p = 0.008). By postoperative day 30, no statistically significant difference in CCT was observed between the groups.

Regarding central macular thickness (CMT), no statistically significant difference was found between the two groups at any of the postoperative follow-up visits.

However, when evaluating the change in CMT from baseline, as shown in **Table (2)**, a statistically significant difference was detected between the two groups on postoperative day 30. The mean ± SD change in CMT in Group A and Group B was 3.68 ± 33.96 µm and 26.0 ± 28.14 µm, respectively (p = 0.017), indicating less postoperative macular thickening among patients treated with nepafenac compared to those treated with prednisolone acetate

Table (1) Ocular Inflammation and Corneal Edema Parameters at Each Postoperative Visit (Mean ± SD)

Parameter	Postoperative Day	Group A (Nepafenac 0.1%)	Group B (Prednisolone acetate 1%)	P-value
AC cells grade	Day 1	2.08 ± 0.70	2.34 ± 0.94	0.260
	Day 4	1.28 ± 0.71	1.56 ± 1.02	0.474
	Day 7	0.92 ± 0.47	1.00 ± 0.65	0.751
	Day 30	0.42 ± 0.34	0.30 ± 0.29	0.217
AC flare grade	Day 1	1.36 ± 0.57	1.44 ± 0.77	0.793
	Day 4	0.68 ± 0.48	1.00 ± 0.50	**0.030***
	Day 7	0.36 ± 0.49	0.52 ± 0.87	0.697
	Day 30	0.00 ± 0.00	0.04 ± 0.20	0.317
Conjunctival hyperemia grade	Day 1	1.12 ± 0.33	1.24 ± 0.52	0.293
	Day 4	0.76 ± 0.52	0.92 ± 0.40	0.210
	Day 7	0.40 ± 0.50	0.48 ± 0.59	0.693
	Day 30	0.08 ± 0.28	0.08 ± 0.28	1.000
Ocular pain score	Day 1	0.48 ± 0.59	0.68 ± 0.69	0.286
	Day 4	0.24 ± 0.44	0.36 ± 0.49	0.359
	Day 7	0.00 ± 0.00	0.00 ± 0.00	1.000
	Day 30	0.00 ± 0.00	0.00 ± 0.00	1.000
Ocular discomfort & photophobia score	Day 1	2.20 ± 0.50	2.44 ± 0.65	0.152
	Day 4	1.52 ± 0.51	1.88 ± 0.83	0.132
	Day 7	1.08 ± 0.64	1.68 ± 0.75	**0.007***
	Day 30	1.08 ± 0.49	1.08 ± 0.49	0.962
Central corneal thickness (µm)	Day 1	547.52 ± 42.19	602.48 ± 98.63	**0.014***
	Day 4	543.40 ± 42.13	580.36 ± 52.02	**0.008***
	Day 7	538.68 ± 36.92	559.28 ± 36.69	0.054

Data presented as mean ± standard deviation (SD). P-values < 0.05 were considered statistically significant and are shown in bold with an asterisk *****

Table (2): Mean Change in Central Macular Thickness (CMT) from Preoperative Values

Postoperative Visit	Group A (Nepafenac 0.1%) Mean ± SD (µm)	Group B (Prednisolone acetate 1%) Mean ± SD (µm)	P-value
Day 7	–1.60 ± 40.53	3.60 ± 22.52	0.240
Day 30	3.68 ± 33.96	26.00 ± 28.14	**0.017***

Data are presented as mean ± standard deviation (SD). Positive values indicate an increase, and negative values indicate a decrease from the preoperative baseline. P-values < 0.05 were considered statistically significant and are shown in bold with an asterisk.*****

Discussion

In the present study, postoperative visual recovery was comparable between the nepafenac and prednisolone groups, with slightly better clinical outcomes observed in patients receiving nepafenac. This aligns with the findings of Singhal et al. (2022), who reported that visual acuity improvement after uncomplicated phacoemulsification was clinically superior with nepafenac compared to prednisolone, although the observed difference did not reach statistical significance. [15].

In terms of intraocular pressure (IOP), transient elevation was noted with topical steroid use, while the nepafenac group demonstrated a more stable postoperative profile. This observation supports the results of Singhal et al. (2022), who found that corticosteroid therapy may transiently increase IOP, whereas NSAID-based regimens maintain safer postoperative pressure levels [15].

Both treatment protocols were similarly effective in managing anterior chamber inflammation after cataract surgery. These findings are consistent with those of Sarkar et al. (2021), who demonstrated comparable anti-inflammatory efficacy between nepafenac and prednisolone following micro-incisional cataract extraction [12].

Corneal recovery, as indicated by central corneal thickness changes, appeared more favorable in the nepafenac group during the early postoperative period. This trend corresponds with the work of Kim et al. (2022), who found that patients receiving NSAIDs experienced less postoperative corneal edema than those treated with corticosteroids [16].

Regarding macular thickness, nepafenac demonstrated a protective effect against postoperative macular swelling, consistent with previous studies by Sarkar et al. (2021) and Singhal et al. (2022), which reported lower central macular thickness values and reduced risk of cystoid macular edema in patients treated with NSAIDs compared to those receiving corticosteroids [12,15].

Overall, our findings suggest that topical nepafenac 0.1% provides comparable anti-inflammatory efficacy to prednisolone acetate 1% following uneventful phacoemulsification, with the added advantages of better corneal and macular stability and a lower tendency for postoperative IOP elevation. These findings support the therapeutic use of nepafenac as a safe and effective alternative to corticosteroids for the treatment of postoperative inflammation after cataract surgery.

The small sample size and brief follow-up period (30 days) are two of the study's limitations. To corroborate these findings, more multicenter studies with bigger sample sizes and longer follow-up times are required.

Conclusion

Topical nepafenac 0.1% demonstrated comparable efficacy to prednisolone acetate 1% in controlling postoperative inflammation following cataract surgery. In addition, nepafenac may provide an added advantage in reducing the likelihood of postoperative cystoid macular edema and intraocular pressure elevation. Consequently, nepafenac 0.1% represents a viable and potentially safer alternative to corticosteroids for postoperative inflammation management, particularly in

patients predisposed to infection, CME, or steroid-induced ocular hypertension.

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