

Comparison of a Preservative-free Non-steroidal Anti-inflammatory Drug and Preservative-free Corticosteroid after Uneventful Cataract Surgery: A Randomized Control Trial

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Abstract

Background: Cataract is considered as a main cause of blindness around the world along with glaucoma and macular degeneration. Now, surgery remains the only effective treatment option of cataracts and cataract surgery is one of the most frequently accomplished surgeries in the field of ophthalmic arena. This study aimed to compare the effects of NSAIDs with those of steroids for the management of inflammation after uneventful cataract surgery. **Methods:** This study was a prospective randomized control trial, conducted at the Department of Cataract in National Institute of Ophthalmology and Hospital, Dhaka, from 01 February 2021- 30 January 2022. A total of 194 patients were randomly allocated into two groups by lottery. The patients of NSAID group was prescribed bromfenac sodium hydrate 0.1% to apply two times a day in 1 eye, whereas the steroid group was treated with Dexamethasone 0.1%, 4 times per day for 4 weeks after the surgery. **Results:** The mean age of the patients in NSAID and steroid group were 71.10 (\pm 8.55) years and 72.09 (\pm 8.64) years respectively. The male female ratio of each group was 33:64. The change in inflammation grade of the anterior from postoperative day 1 to week 8 in the NSAID group was -1.25 ± 1.30 and in the steroid group -1.25 ± 1.32 which shows a significant reduction in both eyes ($p < 0.001$). Comparing the changes from preoperative to week 1 and preoperative to week 8 showed central corneal thickness in the NSAID group was also significantly less than that in the steroid group (8.87 ± 22.46 and 29.48 ± 46.60 vs. 4.74 ± 31.75 and 8.76 ± 40.95 mm) ($p < 0.05$). Comparing the changes from postoperatively to week 1 and postoperatively to week 8, the NSAID group had lower conjunctival hyperemia -0.09 ± 0.53 and -0.19 ± 0.54 vs. the steroid group had higher conjunctival hyperemia 0.08 ± 0.64 and -0.20 ± 0.53 . **Conclusion:** NSAIDs like nepafenac 0.1%, bromfenac 0.09%, and ketorolac 0.5% are proven to be a good alternative to steroids which has a corresponding level of anti-inflammatory activity like Dexamethasone 0.1% for controlling postoperative ocular inflammation among patients going through cataract surgery.

Keywords: Preservative-free Non-steroid, Anti-inflammatory Drug, Preservative-free Corticosteroid, Cataract Surgery.

(*J.Natl.Inst.Ophthalmol.2022;5(1):10-15*)

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Received: 17 Sept. 2022

Accepted: 27 Nov. 2022

Introduction

Cataract is considered as a main cause of blindness around the world along with glaucoma and macular degeneration. The incidence of cataracts is being increased speedily among the elder population. Now, surgery remains the only effective treatment option of cataracts and cataract surgery is one of the most frequently accomplished surgeries in the field of ophthalmic arena. Also the advances in cataract surgery like phacoemulsification using a minimal incision and advancements in surgical equipment and intraocular lenses (IOLs) and ophthalmic viscosurgical devices had lessen the risk for physical strain and post-operative complications. However, post-operative irritation resulted by the ocular surface and tear film because of intraoperative influences or presence of

preservatives (eg, benzalkonium chloride) in eyedrops, can lead to the uneasiness and late recovery.¹ Moreover, mismanagement in inflammation control can add more complications like endophthalmitis, cystoid macular edema (CME), and posterior capsule opacity. Hence, proper management is required as complications may disrupt the restoration of normal vision.² Steroids are renowned anti-inflammatory mediators which works through the inhibition of inflammatory response mediator production.³ Steroids have been efficiently used for the management of inflammation after cataract surgery. But, steroid use also has risk for increased intraocular pressure (IOP), postoperative infection.⁴ Prednisolone, dexamethasone, Dexamethasone, and loteprednol are the generally used steroids. Nonsteroidal anti-inflammatory drug (NSAIDs) are another type of anti-inflammatory mediators. In contrast to steroid eyedrops, NSAIDs do not rise the IOP or the risk for infection. Besides, NSAIDs has mitotic reticence and have painkilling properties during surgery.⁵ Moreover, studies have confirmed the benefits of NSAIDs in avoiding CME after cataract surgery.^{6,7} Now, ketorolac, diclofenac, and bromfenac are used widely. Bromfenac may increases the penetrability of ocular tissues and prolongs the time of action of amfenac due to the accumulation of a bromide group to the prevailing amfenac formulation.⁸ It spreads in retina concentrations which is required for the avoidance of CME by only applying two times a day, whereas other similar drugs needs to applied 3 to 4 times.⁹ Studies have estimated the efficacy and safety of NSAIDs in comparison with those of steroids for the controlling of post-operative inflammation.^{6,7,10} Though NSAIDs have a superior anti-inflammatory effect on anterior flare as evaluated by flow cytometry, but it is nearly impossible to practice clinically.^{11,12} Hence, this study aimed to compare the effects of NSAIDs with those of steroids for the management of inflammation after uneventful cataract surgery based on anterior inflammatory and corneal conjunctival indicators using a slitlamp examination.

Methods

This study was a prospective randomized control trial, conducted at the Department of Ophthalmology in National Institute of Ophthalmology and Hospital, Dhaka, during the period of 01 February 2021- 30 January 2022. The total sample size for this study was 194.

Inclusion criteria

1. Adult patients >50 years
2. Patients with age-related cataracts and decided to undergo cataract surgery in both eyes
3. Patients with cataracts of grades 3 to 4 with nuclear sclerosis and
4. Patients with preoperative endothelial cell count of ≥ 1500 cells/mm

Exclusion criteria

1. Patients who had the history of eye trauma or corneal transplantation
2. Patients with congenital cataract, aniridia, iris atrophy, pseudoexfoliation syndrome, and other retinal disease which can affect vision like diabetic retinopathy, epiretinal membrane, and macular edema
3. Patients who were administered by other eyedrops for therapeutic purposes within 2 weeks of cataract surgery and had chronic or recurrent ocular inflammatory disease like uveitis or scleritis, glaucoma, allergy, or dry eye disease which requires treatment other than artificial tears
4. Patients with uncontrolled diabetes or hypertension
5. Patients receiving systemic NSAIDs or steroids within 2 weeks of cataract surgery or those who might need those during the clinical trial period
6. Patients having the experience of surgical complications like posterior capsular rupture or vitreous prolapse during surgery or any active inflammatory treatment required postoperatively

Randomization

Patients were randomly allocated into two groups by lottery. The patients of NSAID group was prescribed bromfenac sodium hydrate 0.1% to apply two times a day in 1 eye, whereas the steroid group was treated with Dexamethasone

0.1%, 4 times per day for 4 weeks after the surgery. The major efficacy outcome was the existence of anterior chamber cells and flare at 1 week after the surgery. The secondary outcomes were anterior chamber cells and flare at 4 to 8 weeks, corrected distance visual acuity, central corneal thickness, conjunctival hyperemia, dry eye parameters, foveal thickness, and ocular and visual discomfort. The patients were enrolled in this study after taking the written consent from

them. All the data during the whole treatment course were recorded properly. The ethical approval was given by the ethical review committee. The statistical analysis was done using the statistical tool SPSS version 21. Chi-square test, independent sample t test and paired t-test were used to identify the difference between the two groups. The level of significance was assessed at $p < 0.05$.

Results

Table I: Demographic and baseline clinical characteristics of patients (n=194)

Demographic	NSAID group (n = 97) mean \pm SD	Steroid group (n = 97) mean \pm SD	P value
Age	71.10 \pm 8.55	72.09 \pm 8.64	0.082 ^a
Male: Female	33:64	33:64	0.093 ^b
UDVA (logMAR)	0.43 \pm 0.26	0.45 \pm 0.23	0.5760 ^a
CDVA (logMAR)	0.37 \pm 0.29	0.41 \pm 0.30	0.3174 ^a
IOP (mm Hg)	15.24 \pm 3.35	15.31 \pm 3.99	0.8760 ^a
Keratoconjunctiva			
Oxford staining	0.26 \pm 0.58	0.23 \pm 0.51	0.4532 ^a
TBUT(s)	6.28 \pm 2.10	6.24 \pm 2.08	0.8422 ^a
CCT (mm)	540.47 \pm 40.51	535.65 \pm 46.72	0.0903 ^a
ECD (cells/mm ²)	2642.81 \pm 369.27	2624.32 \pm 378.61	0.6100 ^a
Macular			
Foveal thickness (mm)	246.50 \pm 39.58	246.14 \pm 40.14	0.5622 ^a
Lens			
Nucleus (N)	4.32 \pm 0.47	4.31 \pm 0.47	1.0000 ^a
Cortex (C)	4.07 \pm 1.29	4.11 \pm 1.31	0.5445 ^a
Posterior capsule (P)	0.00 \pm 0.00	0.00 \pm 0.00	
Phacoemulsification			
Time (s)	33.79 \pm 25.94	34.73 \pm 24.81	0.3439 ^a
Power (%)	23.02 \pm 15.36	22.81 \pm 15.35	0.2304 ^a

a=Independent sample t test, b=chi-square test

UDVA: Uncorrected Distance Visual Acuity, CDVA: Corrected Distance Visual Acuity, IOP: Intraocular pressure, TBUT: Tear Break Up Time, CCT: Central corneal thickness, ECD: endothelial cell density

The mean age of the patients in NSAID group was 71.10 \pm 8.55 years and in Steroid group was 72.09 \pm 8.64 years. The male female ratio of each group was 33:64. No statistically significant differences were found in any of the two groups in respect of visual acuity, IOP, corneal conjunctiva, TBUT(s), ECD (cells/mm²), macular and phacoemulsification status at the time of surgery (table I).

Table II: Change in Inflammation Grade of Anterior Chamber

Period	NSAID group mean \pm SD	Intragroup p value	Steroid group mean \pm SD	Intragroup p value	Intergroup P value
1 day	1.25 \pm 1.29		1.26 \pm 1.34		0.989 ^a
1 week	0.22 \pm 0.40		0.31 \pm 0.65		0.174 ^a
4 week	0.05 \pm 0.17		0.07 \pm 0.25		0.703 ^a
8 week	0.02 \pm 0.05		0.02 \pm 0.10		0.999 ^a
Δ 1 week to 1 day	-1.04 \pm 1.27	<0.001 ^b	-0.96 \pm 1.24	<0.001 ^b	0.485 ^a
Δ 4 week to 1 day	-1.21 \pm 1.31	<0.001 ^b	-1.20 \pm 1.30	<0.001 ^b	0.750 ^a
Δ 8 week to 1 day	-1.25 \pm 1.30	<0.001 ^b	-1.25 \pm 1.32	<0.001 ^b	0.947 ^a

a=Independent sample t test, b=paired t test

The change in inflammation grade of the anterior from postoperative day 1 to week 1 in the NSAID group was -1.04 ± 1.27 and in the steroid group -0.96 ± 1.24 where these changes from postoperative day 1 to week 8 in the NSAID group was -1.25 ± 1.30 and in the steroid group -1.25 ± 1.32 which shows a significant reduction in both eyes ($p < 0.001$) (table II).

Table III: Change in Central Corneal Thickness

Period	NSAID group mean \pm SD	Intra- group p value	Steroid group mean \pm SD	Intragroup p value	Inter- group p value
1 day	549.47 \pm 40.51		535.65 \pm 46.72		0.0903 ^a
1 week	548.34 \pm 48.81		565.12 \pm 48.41		<0.001 ^a
4 week	548.01 \pm 37.49		548.85 \pm 39.85		0.241 ^a
8 week	545.20 \pm 37.00		544.39 \pm 39.73		0.962 ^a
Δ 1 week to preoperative	8.87 \pm 22.46	0.007 ^b	29.48 \pm 46.60	<0.001 ^b	<0.001 ^a
Δ 4 week to preoperative	5.33 \pm 18.93	0.065 ^b	10.17 \pm 23.28	<0.001 ^b	0.007 ^a
Δ 8 week to preoperative	4.74 \pm 31.75	0.167 ^b	8.76 \pm 40.95	0.017 ^b	0.081 ^a

a=Independent sample t test, b=paired t test

Comparing the changes from preoperative to week 1 and preoperative to week 8 showed central corneal thickness in the NSAID group was also significantly less than that in the steroid group (8.87 ± 22.46 and 29.48 ± 46.60 vs. 4.74 ± 31.75 and 8.76 ± 40.95 mm ($p < 0.05$)) (table III).

Table IV: Change in Conjunctival Injection

Period	NSAID group mean \pm SD	Intra- group p value	Steroid group mean \pm SD	Intra- group p value	Intergroup p value
Preoperative	0.38 \pm 0.78		0.38 \pm 0.75		0.999 ^a
1 day	0.87 \pm 1.01		0.88 \pm 0.99		0.894 ^a
1 week	0.31 \pm 0.52		0.45 \pm 0.81		0.014 ^a
4 week	0.25 \pm 0.57		0.25 \pm 0.61		0.999 ^a
8 week	0.21 \pm 0.53		0.19 \pm 0.46		0.625 ^a
Δ 1 week to postoperatively	-0.09 \pm 0.53	0.1317 ^b	0.08 \pm 0.64	0.320 ^b	0.011 ^a
Δ 4 week to postoperatively	-0.15 \pm 0.50	0.0079 ^b	-0.14 \pm 0.51	0.008 ^b	0.999 ^a
Δ 8 week to postoperatively	-0.19 \pm 0.54	0.0011 ^b	-0.20 \pm 0.53	0.005 ^b	0.999 ^a

Comparing the changes from postoperatively to week 1 and postoperatively to week 8, the NSAID group had lower conjunctival hyperemia -0.09 ± 0.53 and -0.19 ± 0.54 vs. the steroid group had higher conjunctival hyperemia 0.08 ± 0.64 and -0.20 ± 0.53 (table IV).

Discussion

This study was carried out to evaluate the effects of NSAIDs and corticosteroids after cataract surgery focusing on anterior inflammatory indicators by using slitlamps, as this can simply be functioned in realistic environment. The drugs including Bronuck, bromfenac sodium hydrate solution 0.1% that was given two times a day and for anterior chamber inflammation, Dexamethasone solution 0.1% were also given 4 times every day. Bronuck resulted improve corneal conjunctival indicators and awkwardness postoperatively. Studies had tried to find the possibility of replacing a corticosteroid used with an NSAID for managing the inflammation after cataract surgery. 6, 7, 10, 11, 12, 14 A meta-analysis observed comparatively low flare of the anterior chamber and a less risk for developing CME in the NSAID group than the corticosteroid group. But, it was not confirm that whether the number of cells was higher or lower and whether there was a higher prevalence of corneal swelling. Furthermore, some studies in this field had also defined the intraocular cell and flare and corneal edema. In this present study, the anterior chamber inflammation grade was assessed using the SUN criteria under slitlamps. In a study, the percentage was found 4.0% among patients with residual anterior chamber inflammation based on slitlamp examination in the bromfenac group whereas it was 4.4% in the dexamethasone group at 6 weeks after the surgery.¹⁴ Similarly in this study, the effects of bromfenac 0.1% and Dexamethasone 0.1% on anterior chamber inflammation were found effective. Comparing the changes from preoperative to week 1 and preoperative to week 8 showed central corneal thickness in the NSAID group was also significantly less than that in the steroid group (8.87 ± 22.46 and 29.48 ± 46.60 vs. 4.74 ± 31.75 and 8.76 ± 40.95 mm ($p < 0.05$). Moreover, bromfenac showed effective results in eye dryness postoperatively than that of using Dexamethasone. In the study of Fujishima et al. bromfenac sodium ophthalmic solution had also reported to improve eye dryness, especially,

TBUT and corneal effects.¹⁵ Comparing the changes from postoperatively to week 1 and postoperatively to week 8, the NSAID group had lower conjunctival hyperemia -0.09 ± 0.53 and -0.19 ± 0.54 vs. the steroid group had higher conjunctival hyperemia 0.08 ± 0.64 and -0.20 ± 0.53 .

Conclusion

NSAIDs like nepafenac 0.1%, bromfenac 0.09%, and ketorolac 0.5% are proven to be a good alternative to steroids which has an corresponding level of anti-inflammatory activity like Dexamethasone 0.1% for controlling postoperative ocular inflammation among patients going through cataract surgery. Besides, all these four drugs are also operative in controlling post-cataract surgery ocular inflammation. Though, intraocular inflammation can be predominantly controlled with Dexamethasone 1%, but ocular pain and hyperemia are well controlled with NSAIDs in the early postoperative phases. Hence, for a better result on improving various keratoconjunctival signs and symptoms after cataract surgery and better compliance, tolerability and reduced complications, NSAIDs is suggested to use effectively for the treatment of inflammation after simple cataract surgery.

Conflict of Interest: Nothing to declare.

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