

## A Comparative Study of Various Topical Nonsteroidal Anti-Inflammatory Drugs to Steroid Drops for Control of Post Phacoemulsification Surgery Inflammation

A.M.Hegazy, S.R.Abbas, A.A.Alshayeb and M.G.Shaarawy  
Ophthalmology, Dept., Faculty of Medicine, Benha Univ., Benha, Egypt  
Email: [dr.am86@yahoo.com](mailto:dr.am86@yahoo.com)

### Abstract

In the past, patients who underwent cataract surgery were prescribed an antibiotic drop and a topical steroid to reduce inflammation in the days following the procedure. However, steroids can have negative consequences, such as slowed wound healing, increased susceptibility to infection, and increased intraocular pressure (IOP) that can cause permanent damage to the optic nerve. Bromfenac is an NSAID that has been demonstrated to reduce post-operative pain and inflammation and is associated with better adherence (since it needs to be taken less frequently) and fewer adverse effects. The purpose of this research was to evaluate the efficacy of a topical steroid against a topical NSAID in the prevention and treatment of inflammation following phacoemulsification surgery. Methods: Eighty eyes from eighty patients who had conventional uncomplicated phaco emulsification with posterior chamber intra ocular lens implantation were used in this prospective randomised study comparing the effect of topical non-steroidal anti-inflammatory drugs versus steroidal drugs in preventing post-operative inflammation following phaco emulsification surgery. Patients were randomly assigned to one of two groups based on whether they received oral or topical medication for the first three weeks after surgery. Twenty patients were assigned to Group A, where they received prednisolone 1% eye drops every two hours for the first week, four times a day for the second week, twice a day for the third week, and gatifloxacin 0.3% six times a day for the entire two weeks. For those in B-Group: For Group B, we divided 60 eyes into three categories: Group B1 received eye drops containing 0.1% diclofenac sodium, while Group B2 received eye drops containing 0.1% nepafenac. The Bromfenac 0.1%.eye drop group B3 treated 20 eyes. While the first week showed statistically significant differences in corneal edoema, anterior chamber cells, and flare, by the third week the results were similar across all four groups. In terms of eyesight, we also discovered a statistically significant difference between Group A and Groups B1, B2, and B3, but this difference had diminished by the third visit. Up to the last visit of the third week, there was no significant difference between the four groups' IOP measurements. Our data demonstrated a marginally different response to steroid or NSAID use, with the steroid group experiencing less corneal edoema than the NSAID group up to the third week visit. Patients undergoing phacoemulsification surgery can benefit from nonsteroidal anti-inflammatory drugs (NSAIDs) like nepafenac 0.1%, bromfenac 0.1%, and Diclofenac sodium 0.1% instead of steroids for postoperative ocular inflammation control. Intraocular inflammation is best treated with prednisolone 1% as it achieved reduced AC cells and flare.

**Key words:** Topical Nonsteroidal Anti-Inflammatory Drugs, Steroid Drops, Post Phacoemulsification Surgery Inflammation.

### 1. Introduction

The success of cataract surgery relies on the surgeon and patient making the proper choice in anti-inflammatory medication. To alleviate eye inflammation, anti-inflammatory drugs, both steroidal and nonsteroidal, might be helpful (NSAIDs). Reduced inflammation may be achieved with the use of either steroids or nonsteroidal anti-inflammatory drugs (NSAIDs), with steroids acting on various intercellular inflammatory mediators and NSAIDs inhibiting the enzymes responsible for producing cyclooxygenase. Prostaglandins may be synthesised due to the cyclooxygenase enzymes. Inflammation is reduced when prostaglandin production is suppressed [1].

Measurements of intraocular pressure (IOP), inflammatory indicators (including conjunctival hyperemia, ocular discomfort, aqueous cells, and flare), and ocular pain were taken to draw comparisons between the medications. The rate at which cells in the anterior chamber reduced was considered as the key measure of effectiveness. Slit-lamp examination indicated a continuous drop in the number of cells in the anterior chamber commencing on the second postoperative day, suggesting that the inflammatory response was under control in all four groups. Previous study has indicated

that gradual tapering of topical ocular steroid usage is superior in reducing ocular rebound inflammation that may emerge as a consequence of fast tapering or abrupt withdrawal of steroid therapy. [2] It's unknown what mechanisms could contribute to a return of ocular illness after a patient stops taking steroids. [2] Topical corticosteroids are often used as normal therapy for many weeks after cataract surgery to reduce the inflammatory reaction. The goal of this research was to investigate the relative safety and effectiveness of steroid and nonsteroidal anti-inflammatory medication (NSAID) drops for lowering inflammation following cataract surgery.

### 2. Patients and Methods

This is prospective randomized study in which we compared the effect of topical non-steroidal anti-inflammatory drugs versus steroidal drugs in prevention of post-operative inflammation after phaco emulsification surgery, it was conducted on 80 eyes of 80 patients who had cataract extraction using conventional uncomplicated phacoemulsification with posterior chamber intra ocular lens implantation

Patients have been randomized to receive NSAIDs drops or steroid drops.

The study was performed between October 2018 and September 2019.

All patients were recruited from Outpatient Clinic of Benha University Hospital.

### **2.1 Inclusion criteria:**

- 1- Cases of senile cataract.
- 2- Age above 40 years.

### **2.2 Exclusion criteria:**

1. Topical/ inhaled / systemic steroid 14 days before surgery.
2. Topical / Inhaled / Systemic NSAIDs within 7 days.
3. Patient with past history of iritis.
4. Corneal opacity.
5. Suspected hypersensitivity to NSAIDs.
6. Chronic or recurrent inflammatory eye disease.
7. Diabetic patient.
8. Sever dry eye patient.
9. Glaucoma patient.
10. Patient having posterior segment pathology.

**Patients that had any intra-operative complication excluded from this study.**

All participants received a thorough explanation of the study design and aims.

Study participants were asked to sign an informed consent before an initiation of study- related procedures.

**Every patient included in the study was subjected to:**

#### **A- A complete ophthalmic history including:**

- Age.
- History of systemic diseases.
- History of previous eye surgery or trauma.
- Previous topical or systemic medications.

#### **B- Ophthalmic examination including:**

- Preoperative measuring of uncorrected visual acuity (UCVA) and best corrected visual acuity (BCVA) preoperative using Landolt C chart and expressed as logMAR.

Examination of ocular adnexa including the eye lids, conjunctiva, lacrimal system and orbit.

- Intra ocular pressure using Goldmann applanation tonometer.
- Anterior segment detailed slit lamp examination.
- Fundus examination by indirect ophthalmoscopy.

Biometry was performed to calculate IOL power by: (Sonomed Escalon FB, PacScan model 300A+, New York, USA) on of study – related procedures.

Patients divided into two groups according to the treatment with topical drugs for 3 weeks postoperative.

#### **Group A:**

Was 20 patients treated with prednisolone 1% eye drops every 2 hours in the first week, 4 times/ daily in the second week, 2 times/ daily in the third week and gatifloxacin 0.3% six times / day for 2 weeks.

#### **Group B:**

▪ **Group B** was 60 eyes and classified into 3 groups:

▪ **Group B1** 20 eyes treated with Diclofenac sodium 0.1% eye drops.

▪ **Group B2** 20 eyes treated with Nepafenac 0.1% eye drops .

▪ **Group B3** 20 eyes treated with Bromfenac 0.1% eye drops.

#### **The treatment regimen was using the eye drops:**

Every 2 hours in the first week, 4 times daily in the second week, 2 times/ daily in the third week in addition Gatifloxacin 0.3% eye drops was used six times / day for 2 weeks.

#### **Surgical procedure:**

##### **A. Preoperative preparation:**

On the day of the operation, 30 minutes preoperatively, the pupil was dilated by topical application of Mydracil (tropicamide 1 %, Alcon Laboratories, Inc., USA). Before surgery, the phaco machine was set to suitable parameters according to anterior chamber depth, nucleus hardness and surgeon preferences all operations done under local anesthesia.

##### **B. Operative details:**

All patients underwent standard phacomulsification technique using InVivoSight machine (Alcon, Fort Worth, Texas, USA) with special emphasis on the following:

- Capsulorrhexis
- Cortical-cleaving hydrodissection.
- Nucleus emulsification
- Cortical cleanup.
- Foldable acrylic IOL with 6.0 mm optic diameter and 12.5 mm haptic diameter implantation in bag.

##### **C-Post operative treatment:**

▪ Topical broad spectrum antibiotic: Tymer (0.3% gatifloxacin, Jamjoom Pharmaceuticals, Jeddah-Saudi Arabia.) eye drops 6 times per day for two weeks.

▪ Group A treated by steroid eye drops: Predfort (1% prednisolone acetate: Allergan Pharmaceutical, Irvine, Calif) every 2 hours in the first week, 4 times daily in the second week, 2 times/ daily in the third week.

▪ Group B1 treated by NSAIDs eye drops: Epifenac (Diclofenac sodium 0.1% Egyptian Int. Pharmaceutical Eipico 10th of Ramadan city industrial area B1) by the same regimen as group A.

▪ Group B2 treated by NSAIDs eye drops: NEVANAC® (nepafenac 0.1%; Alcon Research, Ltd., Fort Worth, TX, USA) by the same regimen as group A.

▪ Group B3 treated by NSAIDs eye drops: Bromoflam: ( bromfenac 0.09% Orchidia Pharmaceutical Industries- Egypt ) by the same regimen as group A.

##### **Postoperative evaluation:**

Follow-up of patients was performed on the first day, first week, second week and third week

postoperatively, with a full ophthalmic examination at each visit.

Anterior segment examination using slit lamp biomicroscopy. To detect postoperative inflammation in the form of corneal edema and anterior chamber reaction in the form of flare and cells.

Grading of anterior chamber cells with narrowest slit of slit lamp (1mm wide-1mm height).

The number of cells per high power field in the anterior chamber will be counted and recorded on scale according to:

**(SUN) scale grading system:**

- Grade 0 no cells
- Grade 0.5 1-5 cells
- Grade 1 represented 5-10 cells
- Grade 2 represented 11-20 cells
- Grade 3 represented 21-50 cells
- Grade 4 represented ≥ 50 cell

Grading of flare also according to:

**(SUN) grading 5 points scale.**

- Grade 0 none
- Grade 1+ faint
- Grade 2+ moderate (iris+ lens clear)
- Grade 3+ marked (iris+ lens hazy)
- Grade 4+ intense (fibrin or plastic aqueous)

Cornea examined for clarity or presence of edema

Intra ocular pressure was measured using goldmann applanation tonometer.

Conjunctival hyperemia also noticed and classified from 0 to 4+. Fundoscopy also done in the post operative follow up.

Visual acuity examination done with recording BCVA in all visits.

Patients also asked to subjectively rank their pain on a six-point scale from 0(none) to5(sever),according to verbal rating scale(VRS).

They also asked about photophobia, burning sensation.

**STATISTICAL ANALYSIS**

The clinical data were recorded on a report form. These data were tabulated and analysed using the computer program SPSS (Statistical package for social science) version 20 to obtain:

**DESCRIPTIVE DATA**

**Descriptive statistics were calculated for the data in the form of:**

**1.** Mean and standard deviation □ □ SD□. for quantitative data.

**2.** Frequency and distribution for qualitative data

**Analytical Statistics**

In the statistical comparison between the different groups, the significance of difference was tested using one of the following tests

**1.** ANOVA test (F value):-Used to compare mean of more than two groups of quantitative data.

Inter-group comparison of categorical data was performed by using

**2.** Chi square test (X2-value) and fisher exact test (FET).

**3. Results**

**Table (1)** the mean IOP at various time intervals:

IOP	GP A		GP B1		GP B2		GP B3		Statistic altest (F)	P value
	mea	SD	mea	SD	mea	SD	mea	SD		
	n	n	n	n	n	n	n	n		
IOP	16.3	1.72	15.7	2.36	15.8	2.06	16.1	2.03	0.36	0.79
1 <sup>st</sup> d	15.1	2.22	14.8	2.5	15.4	2.26	15.7	1.78	0.62	0.61
1 <sup>st</sup> w	15.4	1.85	15.4	2.04	15.7	1.92	16.1	1.79	0.60	0.62
2 <sup>nd</sup> w	16.7	1.65	15.9	2.1	15.8	2.11	16.1	1.97	0.89	0.45
3 <sup>rd</sup> w	17.3	1.59	15.9	2.13	16.2	2.28	16.3	1.81	1.9	0.14

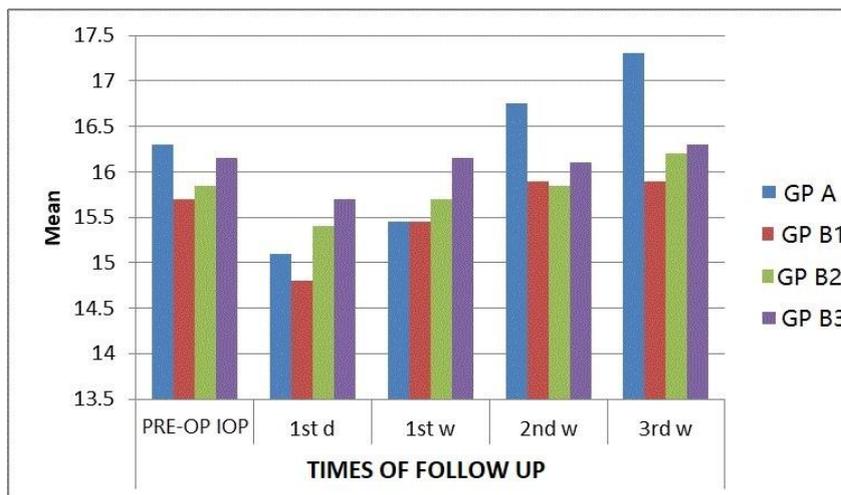


Fig. (1) The mean IOP at various time intervals.

The mean IOP at various time intervals was comparable in all groups of our study. We observed that the difference in IOP at various time intervals among the four groups was not significant [Table 1]

Table (2) Ac-flare in the four groups.

Ac flare	Time Interval	GP A		GP B1		GP B2		GP B3		Statistical test	P value	
		N	%	N	%	N	%	N	%			
Ac flare	1 <sup>st</sup> d	0	1	5	6	3	6	3	5	FET= 12.13	0.40	
		1	3	1	6	1	8	5	9			
		2	5	5%	5	5	5%	5	4			4
		3	1	2	0	3	3	4	1			45
		4	0	5%	0	0	0%	0	0			0
	1 <sup>st</sup> w	0	5	0	5	2	2	2	20	FET= 18.04	9*	
		1	6	0%	4	5%	7	5%	7			35
		2	3	0%	3	2	5	4	4			35
		3	0	1	0	1	0	2	2			20
		4	0	5%	0	5%	5%	0	0			10
2 <sup>nd</sup> w	0	7	8	1	6	1	7	1	70	FET= 10.63	0.20	
	1	3	1	4	2	6	3	4	20			
	2	0	5%	4	0%	6	0%	1	5			
	3	0	0	0	2	0	0	1	5			
	4	0	0	0	0	0	0	0	5			
3 <sup>rd</sup> w	0	0	0	0	0	0	0	0	5			
	1	0	0	0	0	0	0	0	5			
	2	0	0	0	0	0	0	0	5			
	3	0	0	0	0	0	0	0	5			
	4	0	0	0	0	0	0	0	5			

w	1	9	1	7	1	9	1	85	FET=	0.35
0	9	5%	5	5%	8	0%	7	%	6.30	
1	1	5	5	2	2	1	2	10		
2	0	%	0	5%	(	0%	1	%		
		0		0		0		5		
		%		%		%		%		

The overall anterior chamber flare grades at the 1st day were comparable, and there was no statistically significant difference between all groups in the 1st day. However, it was observed that there was a significant difference between group A and the other three groups in the 1st week (P value 0.019). But the overall anterior chamber flare grades at the 2nd and 3rd week were comparable between all groups.

#### 4. Discussion

IOP was normal at all four visits for patients receiving 0.1% diclofenac sodium, and the medicine was also shown to be effective in relieving postoperative ocular discomfort and inflammation without creating any serious safety concerns. Demco et al. [4] found that diclofenac sodium 0.01% ophthalmic solution was just as effective, safe, and well-tolerated as prednisolone acetate 1.0% ocular suspension. Studies by elHarazi et al. suggest that ketorolac tromethamine 0.5% and diclofenac sodium 0.1% may be just as effective and safe as prednisolone acetate 1% in treating inflammation after cataract surgery [5].

One hundred percent of patients in the group that used nepafenac 0.1% had normal IOP at all four visits. Furthermore, we learned that nepafenac is an efficient and safe method for treating postoperative ocular inflammation and pain. Two studies found that nepafenac 0.1% was more effective than placebo in preventing and treating ocular irritation: one by Lane et al. [6] and another by Stewart et al. [7].

With the use of bromfenac 0.09%, we found that all patients' IOP remained within the normal range during all visits. Bromfenac 0.09% ophthalmic solution was effective for the rapid treatment of ocular discomfort after cataract surgery, as was shown in a previous research by Donnenfeld et al. [8]. Monitoring aqueous flare levels, Kawaguchi et al. [9] found that bromfenac's anti-inflammatory effects kicked in faster than diclofenac's, and that bromfenac's group consistently had less flare than diclofenac's. Our findings demonstrate that prednisolone 1% is superior to placebo in reducing postoperative intraocular inflammation-induced anterior chamber cells and flare. It was also shown that prednisolone 1% was more successful in treating ocular edema.

On day 7, ketorolac was more effective than prednisolone acetate in reducing intraocular inflammation after cataract surgery, but on days 7 and 28, prednisolone acetate was more useful. Both Maca et al. [12] and Hozler et al. [11] reached the same outcome, although Maca et al. [12] and Hozler et al. [11] found that topical NSAIDs were more palatable; this suggests that both forms of topical medications were similarly helpful in avoiding edema. Meanwhile, a research by Asano et al. found that the use of nonsteroidal anti-inflammatory medicines was linked to decreased inflammation and edema [13].

Nonsteroidal anti-inflammatory medicines (NSAIDs) were shown to be more effective than steroid eye drops in decreasing postoperative inflammation, as measured by laser flare photometry 1 week after surgery, in a comprehensive review by Kessel et al. [14]. Steroids of moderate to high potency (betamethasone, dexamethasone, loteprednol, and prednisolone) were equally effective as NSAIDs in decreasing inflammation, but steroids of low potency (fluorometholone) were much less effective [15].

#### 5. Conclusion

Nonsteroidal anti-inflammatory medications (NSAIDs) such as nepafenac 0.1%, bromfenac 0.1%, and Diclofenac sodium 0.1% are excellent alternatives to steroids for treating postoperative ocular inflammation in patients undergoing phacoemulsification surgery. Due to its ability to decrease both AC cells and flare, prednisolone 1% is the best therapy for intraocular inflammation.

#### 6. References

- [1] **G. Gulkilik, S. Kocabora, M. Taskapili, G. Engin** Cystoid macular edema after phacoemulsification: risk factors and effect on visual acuity. *Can J Ophthalmol*.vol.41,PP.699–703,2006.
- [2] **L. Renfro, JS. Snow** Ocular effects of topical and systemic steroids. *Dermatol Clin*.vol.10,pp.505-12,1992.
- [3] **CG. 51.Laurell, C. Zetterström** Effects of dexamethasone, diclofenac, or placebo on the inflammatory response after cataract surgery. *Br J Ophthalmol*.vol.86,pp.1380-4,2002.
- [4] **TA. Demco, H. Sutton, CJ. Demco, PS. Raj.** Topical diclofenac sodium compared with prednisolone acetate after phacoemulsification-lens implant surgery. *Eur J Ophthalmol*.vol.7,pp.236-40,1997.
- [5] **SM. el- Harazi, RS. Ruiz, RM. Feldman, G. Villanueva, AZ. Chuang.** 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*.vol.29,pp.539-44,1998.
- [6] **SS. Lane, SS. Modi, RP. Lehmann, EJ. Holland.** Nepafenac ophthalmic suspension 0.1% for the prevention and treatment of ocular inflammation

- associated with cataract surgery. *J Cataract Refract Surg*.vol.33,pp.53-8,2007.
- [7] **WC. Stewart, R. Stewart, WA. Maxwell.** Preoperative and postoperative clinical evaluation of nepafenac 0.1% ophthalmic suspension for postcataract inflammation. Presented at: American Society of Cataract and Refractive Surgery; 18 April, 2005. Washington, DC; 2005,2005.
- [8] **ED. Donnenfeld, EJ. Holland, RH. Stewart, JA. Gow, LR. Grillone;** Bromfenac Ophthalmic Solution 0.09% (Xibrom) Study Group. Bromfenac ophthalmic solution 0.09% (Xibrom) for postoperative ocular pain and inflammation. *Ophthalmology*.vol.114,pp.1653-62,2007.
- [9] **T. Kawaguchi, T. Kida, S. Nemoto.** Effect of bromfenac ophthalmic solution on ocular inflammation and corneal epithelial barrier function following cataract surgery. *Folia Ophthalmol Jpn*.vol.54,pp.276-9,2003.
- [10] **JN. Simone, RA. Pendelton, JE. Jenkins** Comparison of the efficacy and safety of ketorolac tromethamine 0.5% and prednisolone acetate 1% after cataract surgery. *J Cataract Refract Surg*.vol.25,pp.699-704,1999.
- [11] **MP. Hozler, KD. Solomon, HP. Sandoval, DT. Vroman.** Comparison of ketorolac tromethamine 0.5% and loteprednol etabonate 0.5% for inflammation after **phacoemulsification: prospective randomized doublemasked study.** *J Cataract Refract Surg*.vol.28,pp.93–99,2002.
- [12] **SM. Maca, M. Amon, O. Findl, G. Kahraman, T. Barisani-Asenbauer.** Efficacy and tolerability of preservative-free and preserved diclofenac and preserved ketorolac eyedrops after cataract surgery. *Am J Ophthalmol*.vol.149,pp.777–784,2010.
- [13] **S. Asano, K. Miyake, I. Ota, G. Sugita, W. Kimura, Y. Sakka, N. Yabe** Reducing angiographic cystoid macular edema and blood-aqueous barrier disruption after small-incision phacoemulsification and foldable intraocular lens implantation: multicenter prospective randomized comparison of topical diclofenac 0.1% and betamethasone 0.1%. *J Cataract Refract Surg*.vol.34,pp.57–63,2008.
- [14] **L. Kessel, B. Tendal, KJ. Jorgensen, D. Erngaard, P. Flesner, JL. Andresen, J. Hjortdal** Post-cataract prevention of inflammation and macular edema by steroid and nonsteroidal anti-inflammatory eye drops. *Am J Ophthalmol*.vol.121,pp.1915–1924,2014.
- [15] **P. Duan, Y. Liu, J. Li.** The comparative efficacy and safety of topical non-steroidal anti-inflammatory drugs for the treatment of anterior chamber inflammation after cataract surgery: a systematic review and network meta-analysis. *Graefes Arch Clin Exp Ophthalmol*.vol.255,pp.639–649,2017.