

Comparison of Topical Nepafenac with Ketorolac Tromethamine in Maintaining Pupillary Dilatation during Phacoemulsification

Salahuddin, Haroon Rashid

ABSTRACT

Background: For good vision, the surgical procedure of choice for cataract is Phacoemulsification nowadays. Proper and adequately dilated pupil is required throughout cataract surgery. Intra-operative miosis increases the risk of complications that are associated with cataract surgery and can result in unexpected surgical outcomes. For required surgical outcome, inflammation control and properly dilated pupil is important during cataract surgery.

Objective: To know which one is more effective, by comparing topical ketorolac tromethamine 0.5% with Nepafenac 0.1%, in the maintenance of pupillary dilatation during phacoemulsification when instilled for 1 hour (1 drop every 15 minutes) before surgery.

Materials and Methods: This study is a Randomized control trial and was carried out at the Ophthalmology department of Saidu Group of Teaching Hospitals, Swat. The study duration was six months, that is from 12/1/2016 to 11/7/2016. A total of 490 eyes were included (that is 245 eyes in group A and 245 in group B), with Nepafenac efficacy equal to 17.32% and that of ketorolac tromethamine equal to 27.89%, in terms of loss of pupil mydriasis from the baseline till the end of phacoemulsification. Power of test is equal to 80% and level of significance is equal to 5%. Moreover, (non-probability) consecutive sampling technique was used in the study.

Results: In this study mean age in both groups, that is Nepafenac(0.1%) group and Ketorolac tromethamine (0.5%) group, was 62 years with standard deviation of ± 2.06 and 64 years with standard deviation of ± 2.87 respectively. Out of the total patients, 55 percent patients were male and 45 percent patients were female in Group A and 57 percent patients were male and 43 percent patients were female in Group B. Furthermore, the efficacy of nepafenac 0.1% was 80% and that of ketorolac tromethamine 0.5% was 68%.

Conclusion: It is concluded from our study that Nepafenac 0.1% is better in terms of efficacy, than ketorolac tromethamine 0.5% in the maintenance of dilated pupil during phacoemulsification.

Key Words: Nepafenac 0.1%, Ketorolac Tromethamine 0.5%, dilated pupil, Phacoemulsification surgery.

This article may be cited as: Salahuddin, Rashid H. Comparison of Topical Nepafenac with Ketorolac Tromethamine in Maintaining Pupillary Dilatation during Phacoemulsification. J Saidu Med Coll Swat. 2022;12(1):11-15. DOI:https://doi.org/10.52206/jsmc.2022.12.1.552

INTRODUCTION

Phacoemulsification is the modern and best surgical technique for cataract¹. As constricted pupil during surgery is associated with complications, so control of inflammation and properly dilated pupil is required during surgery for good results²⁻⁴. Proper pupillary dilatation is achieved commonly by topical or intra cameral use of sympathomimetic, anticholinergic agents, or both. The most commonly used drugs for mydriasis are phenylephrine and tropicamide^{5,6}.

For prevention of reduction in mydriasis during surgery and for treatment and reduction of post-operative inflammation and cystoid macular oedema, NSAIDs eye drops are commonly used topically in cataract surgery now a days^{7,8}. Nepafenac is commonly used NSAID and in our study, we will use both Nepafenac and Ketorolac tromethamine for the maintenance of pupillary dilatation during surgery. Nepafenac also has additive effect on pupil dilatation in diabetic patients⁹. The use of Nepafenac 0.1%, before

starting surgery was helpful in maintaining dilated pupil during phacoemulsification, reported by Cervantes-coste et al in their study. Nepafenac is even more effective than flurbiprofen in maintaining pupillary dilatation, shown by sarkar, saumya et al¹⁰. The reduction in the diameter of pupil after finishing surgery was 0.78 ± 0.51 mm in Nepafenac group V/s 1.59 ± 0.94 mm in control group¹¹. Miosis during cataract surgery is induced by trauma during surgery to the iris and ciliary body, which releases prostaglandins and results in miosis. All NSAIDs are efficacious in maintaining dilated pupil during phacoemulsification cataract surgery¹². Topical NSAIDs inhibits the release of prostaglandins and required dilated pupil status is maintained during surgery, due to which most of the intraoperative complications such as rent in a posterior capsule and lens drop is reduced¹³. Nepafenac is also more effective regarding tolerability in patients, in comparison to ketorolac tromethamine¹⁴. Amfenac is the active form of Nepafenac and is a potent inhibitor of both cyclo-oxygenase-1 and cyclo-oxygenase-2 enzymes¹⁵. Nepafenac is converted to amfenac inside the eyeball by ocular tissues. Nepafenac can easily penetrate the eye ball and is readily available and rapidly bioactivated inside the eye, which make it more specific of all the NSAIDs for the inhibition of prostaglandins formation inside

Swat Medical College, Saidu Sharif Swat.

Correspondence: Dr. Salah Uddin
Swat Medical College, Saidu Sharif, Swat.
Email: dr.salahuddin707@yahoo.com

Received: May 06th 2021 Accepted: October 28th 2021

the eye ball¹⁶. The power of penetration to certain tissues is increased and its toxicity risk over tissues like corneal epithelium in eye is reduced by its pro-activated structure¹⁷.

Ketorolac tromethamine (0.5%) ophthalmic solution and topical Flurbiprofen sodium(0.03%) efficacies were compared by Solomon in prevention of constriction of pupil during phacoemulsification. Ketorolac tromethamine (0.5%) was more potent in the maintenance of dilated pupil during surgery¹⁸. Total reduction in the diameter of the pupil at the end of surgery was compared by measuring pupil diameter at the start of surgery and at the end of surgery (after IOL placement), it showed significant changes in vertical pupillary diameter ($p=0.009$) with the minimal change from the baseline ($8\pm 0.50\text{mm}$) in Nepafenac group. In terms of minimum loss in mydriasis in vertical pupillary plane, the Nepafenac group lost 17.32% mydriasis and the ketorolac tromethamin group lost 27.89% mydriasis, which is a significant difference in comparison to total loss of mydriasis¹⁹. In another study, the mean diameter of pupil at end of surgery was 7.65 ± 0.71 mm in Nepafenac group V/s 6.67 ± 0.97 mm in the placebo group²⁰.

We have planned this study to correlate the efficacy of Nepafenac (0.1%) with Ketorolac tromethamine (0.5%) in the maintenance of dilated pupil during phacoemulsification, when given topically for 1 hour (1 drop every 15 minutes) before surgery.

MATERIALS AND METHODS

This Randomized control trial was carried out at the Ophthalmology department of Saidu Group of Teaching Hospitals, Swat. The duration of the study was from 12/1/2016 to 11/7/2016. Total of 490 eyes were included in the study. Two groups were made that is group A (Nepafenac group) and group B (ketorolac tromethamine group). Each group containing 245 eyes, using nepafenac efficacy equal to 17.32% and that of ketorolac tromethamine equal to 27.89%, in terms of loss of pupil mydriasis from baseline till end of phacoemulsification. Power of test is equal to 80% and level of significance is equal to 5%. All those patients fulfilling the inclusion criteria i.e, having senile cataract, reactive pupil, round pupil, pupil diameter of more than or equal to 8mm at the start of surgery and age ranged from 50-70 years of either gender (male/female) were included via OPD in the study, and those with irregular pupil,

unresponsive pupil, pupil diameter less than 7.5mm at the start of surgery, having pseudoexfoliation and diabetes were excluded from the study. The study was carried out after approval from research and ethical committee of hospital. The consecutive (non-probability) sampling technique was used. All of the patients were informed by taking written informed consent about the advantages and purpose of the study.

After taking complete detailed history including all the details given in the proforma like age, sex, complaint of decrease vision and duration of decrease vision etc, complete examination of every patient was done, that includes anterior segment examination, fundus examination and checking pupillary reactions. Lottery method was used to allocate the patients randomly into two groups. Patients of both the groups received their respective topical drops, as 1 drop every 15 minutes for 1 hour before starting surgery. All the surgeries were performed by the same ophthalmologist. Pupil diameters of each patient were measured with special caliper at the start and at the end of surgery.

All of the information given above was mentioned and recorded in a pre- designed proforma. To control bias in the study, the exclusion criteria was followed strictly.

The data was analyzed by SPSS (version 20) program. Quantitative variables (e.g age and pupil size) were calculated as mean \pm SD and qualitative variables (e.g, sex, efficacy) were presented in the form of frequencies and percentages (%). Stratification of efficacy was done among age, sex and pupil size to see effect alteration. Chi square test was applied for effect modification, keeping p-value =0.05 as significant. The results were shown in the form of graphs and tables.

RESULTS

This study was carried out at Ophthalmology deptment of Saidu Group of Teaching Hospitals, Swat. In which a total of 490 eyes (245 eyes in group A and 245 eyes in group B) were included, to know, which group is more effective in maintaining pupillary dilatation during phacoemulsification.

Age was distributed in the two groups in a way that in Group A, 142(58%) patients were from 50-60 years age and 103(42%) patients were from 61-70 years age range, with a mean of 62 years of age,

with standard deviation of ± 2.06 . Where as in Group B, 147(60%) patients were from 50-60 years age and 98(40%) patients were from 61-70 years age range with a mean of 64 years of age with standard deviation of ± 2.87 . (Table No 1).

Sex distribution in the two groups was in such a way that, in Group A there were 135(55%) patients male and 110(45%) patients female, While in Group B 140(57%) patients were male and 105(43%) patients were female. (Table No 2).

Pupil size recorded at the start of surgery was nearly the same in each group that is 8mm or above and recorded in Group A after cataract surgery was = 7.5 mm in 49(20%) eyes and > 7.5 mm in 196(80%) eyes with a mean pupil size of 8.73 mm with standard deviation of ± 1.83 . Where as in Group B patients the pupil size recorded after cataract surgery was = 7.5 mm in 78(32%) eyes and > 7.5 mm in 167(68%) eyes with a mean pupil size of 7.68 mm with a standard deviation of ± 2.11 .(Table No 4).

Table 1. Distribution Related With Age (n=490)

AGE	GROUP A	GROUP B	P valve
50-60 years	142(58%)	147(60%)	0.0001
61-70 years	103(42%)	98(40%)	
Total	245(100%)	245(100%)	
Mean and SD	62 year ± 2.06	64 year ± 2.87	

Test applied was chi square test

Group A: Nepafenac 0.1% Group B: Ketorolac tromethamine 0.5%

Table 2. Distribution Related With Gender

SEX	GROUP A	GROUP B	P value
Male	135(55%)	140(57%)	0.6490
Female	110(45%)	105(43%)	
Total	245(100%)	245(100%)	

Test applied was chi square test

Group A: Nepafenac 0.1% Group B: Ketorolac tromethamine 0.5%

Table 3. Efficacy Stratification w.r.t. Distribution of Age and Gender

AGE	EFFICACY	GROUP A	GROUP B	P value
50-60 years	Effective	114	100	0.0175
	Not effective	28	47	
Total		142	147	
61-70 years	Effective	82	67	0.0688
	Not effective	21	31	
Total		103	98	
SEX				
Male	Effective	108	96	0.0304
	Not effective	27	44	
Total		135	140	
Female	Effective	88	71	0.0387
	Not effective	22	34	
Total		110	105	

Group A: Nepafenac 0.1% Group B: Ketorolac tromethamine 0.5%
 Effective means, pupil diameter of =7.5mm after IOL implantation.

Table 4. Efficacy Stratification W.R.T Pupil Size

PUPIL SIZE	EFFICACY	GROUP A	GROUP B	P value
> 7.5 mm	Effective	0	0	0.0028 (By chi square test)
	Not effective	49(20%)	78(32%)	
Total		49	78	
> 7.5 mm	Effective	196	167	0.0028 (By chi square test)
	Not effective	0	0	
Total		196(80%)	167(68%)	
Mean and SD		8.73mm ± 1.83	7.68 mm ± 2.11	0.0001 (By T test)

Group A: Nepafenac 0.1% **Group B:** Ketorolac tromethamine 0.5%
Effective means, pupil diameter of =7.5mm after IOL implantation.

DISCUSSION

For better visual outcome, phacoemulsification with placement of intraocular lens in the capsular bag is the best surgical technique for cataract now a days¹. Proper and adequately dilated pupil is required throughout cataract surgery. Intraoperative miosis increases the risk of complications so, adequate pupillary dilatation and inflammation control during cataract surgery is important for required surgical outcome^{3,4}.

Our study showed that, mean age in Group A (Nepafenac 0.1%) was 62 years with standard deviation of ± 2.06, while mean age in Group B (Ketorolac tromethamine 0.5%) was 64 years with standard deviation of ± 2.87. In Group A (Nepafenac 0.1%), 45% patients were female and 55% patients were male. Where as in Group B (Ketorolac tromethamine (0.5%), 43% patients were female and 57% patients were male. Furthermore, Ketorolac tromethamine (0.5%) was effective in 167(68%) of the patients, while that of Nepafenac (0.1%) was effective in 80% of the patients.

Almost same results were shown by another study carried out by Atanis R et al²¹ in which total loss of pupillary dilatation was measured and compared at the start and at the end of the surgery, after IOL implantation, it highlighted the differences in pupillary diameters in vertical plane (p = 0.009) with the smallest change in Nepafenac group from baseline (8±0.50mm). In terms of minimum loss in mydriasis in vertical pupillary plane, the nepafenac group lost 17.32% mydriasis and the Ketorolac tromethamin group lost 27.89% mydriasis, which is a significant difference in comparison to total loss of mydriasis. So it means that nepafenac is more effective in comparison to ketorolac tromethamin in terms of loss of pupillary

dilatation at the end of phacoemulsification, that is 17.32% in nepafenac group and 27.89% in ketorolac tromethamin group.

Similarly Verzosa L et al²², in their study observed similar results in which they included a total of 47 eyes (44 patients) with 34 females and 13 males, with a mean of 66.04 ± 8.87 years of age. At the beginning of surgery, the mean of vertical and horizontal diameters of all the groups were similar. After IOL placement in the capsular bag, both the horizontal (p = 0.012) and vertical (p = 0.012) pupillary mean diameters were significantly largest in the Nepfenac group. Nepafenac 0.1% ophthalmic solution has been identified as more effective inhibitor of pupillary mydriasis reduction during phacoemulsification and maintain proper mydriasis during surgery in comparison to Ketorolac tromethamine ophthalmic solution and placebo.

In another study, the efficacy of topical bromfenac 0.09% and nepafenac 0.1% are compared and found that both are effective in maintaining mydriasis during phacoemulsification than control group. The decrease in pupil diameter was significantly more in control group (25.78%) as compared to bromfenac (3.51%) and nepafenac (3.81%) group²³.

In another article, the loss in pupillary diameter at the end of phacoemulsification was 7.50% with nepafenac, 9.84% with flurbiprofen, 10.09% with ketorolac, and 13.83% with control, which shows that nepafenac group has less decrease in pupil size in comparison to the rest of the groups²⁴.

CONCLUSION

It is concluded from our study that, topical Nepafenac (0.1%) is more potent than ketorolac

tromethamine (0.5%) in the maintenance of dilated pupil during cataract surgery.

REFERENCES

- Nangrejo KM, Satho AA, Pechuho MA, Siddiqui SJ, Abbasi AM. Visual outcome, phacoemulsification versus extracapsular cataract extraction. *Med channel* 2011;17(3):29-31.
- Goldman JM, Karp CL. Adjunct devices for managing challenging cases in cataract surgery, capsular staining and ophthalmic viscosurgical devices. *Curropinophthalmol* 2007;18(1):52-7.
- Zanetti FR, Fulco EA, Chaves FR, Dacosta PAP, Arieta CE, Lira RP. Effect of preoperative use of topical prednisolone acetate, ketorolac tromethamine, nepafenac and placebo on the maintenance of intraoperative mydriasis during cataract surgery:a randomized trial. *Indian J ophthalmol* 2012;60(4):277-81.
- Donnefeld ED. Current use of Non-steroidal anti-inflammatory drugs in the treatment of ocular inflammation related to cataract surgery. *European Ophthalmic Review* 2012;6(3):173-7.
- Alpay A, Canturk Ugurbas S, Aydemir C. Efficiency and safety of phenylephrine and tropicamide used in premature retinopathy: a prospective observational study. *BMC Pediatr* 19, 415 (2019).
- Bhurayanontachai P, Saengkaew S, Apiromruck P, Efficacy of an eye drop mixture for pupillary dilatation: A randomized comparative study, *Journal of Optometry*, Volume 10, Issue 2, 2017, Pages 111-116.
- Waseem M, Humayun S. Comparison of anti-inflammatory activity of dexamethasone and diclofenac- sodium eye drops in phacoemulsification. *Jcoll physicians Surg Pak* 2009; 19(9):570-4.
- Kim SJ, Flash AJ, Jampol LM. Non-steroidal anti-inflammatory drugs in ophthalmology. *Survophthalmol* 2010;55(2):108-33.
- Kiziltoprak H, Koc M, Yetkin E, Tekin K, Inanc M, Ozulken K. Additive Effect of Topical Nepafenac on Mydriasis in Patients With Diabetes Mellitus. *Eye Contact Lens*. 2020 Sep; 46(5):310-313.
- Saumya S. "Comparison of preoperative nepafenac (0.1%) and flurbiprofen (0.03%) eye drops in maintaining mydriasis during small incision cataract surgery in patients with senile cataract: A randomized, double-blind study." *Indian journal of pharmacology* vol. 47,5 (2015): 491-5.
- Cervantes-coste G, Sanchez-castro YG, Orozco-carroll M, Mendoza-schuster E, Velasco-Barona C. Inhibition of surgical induced miosis and prevention of postoperative macular edema with nepafenac. *Clinophthalmol* 2009; 3:219-26.
- Rodríguez-García A, Hernández-Camarena JC, López-Jaime GR, Nava-García JA. Effect of Topical Nonsteroidal Anti-inflammatory Drugs on Pupillary Size During Uncomplicated Cataract Surgery. *J Refract Surg*. 2017 Apr 1; 33(4):236-242.
- Muhtaseb M, Kalhoro A, Ionides A. A system for preoperative stratification of cataract patients according to risk of intraoperative complications : a prospective analysis of 1441 cases. *Br J Ophthalmol* 2004; 88:1242-6.
- 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(3).
- Lane SS. Nepafenac a unique non-steroidal produg. *IntOphthalmolClin* 2006;46:13-20.
- Walters T, Raizman M, Ernest P, et al. In vivo pharmacokinetics and in vitro pharmacokinetics of nepafenac, amfenac, ketorolac and bromfenac. *J cataract refract surg* 2007;33:1539-45.
- Lane SS. Nepafenac : a unique non-steroidal produg. *IntophthalmolClin* 2006; 46:13-20.
- Solomon K, Turkalj JW, Whiteside SB. Topical 0.5% ketorolac vs 0.03% flurbiprofen for inhibition of miosis during cataract surgery. *Arch Ophthalmol* 1997; 115: 1119-1122.
- Atanis R, Tuaño PM, Vicencio J, Martinez MJ, Verzosa L. Effect of topical ketorolac tromethamine and topical nepafenac on maintaining pupillary dilation during phacoemulsification. *PhiliPP J oPhthalmol* 2011; 36(1):23-27.
- Surhio SA, Memon M, Talpur R, Talpur KI. Efficacy of nepafenac 0.1% in maintaining mydriasis during phacoemulsification surgery. *Journal of the Liaquat University of Medical and Health Sciences* 2013; 12(2):74-78.
- Atanis R, Prospero M. Effect of topical ketorolac tromethamine and topical nepafenac on maintaining pupillary dilation during phacoemulsification. *PhiliPP J OPhthalmol*. 2011; 36(1):23-27.
- Verzosa L, Martinez JM, Vicencio J, Tuaño PMA. Effect of topical ketorolac tromethamine and topical nepafenac on maintaining pupillary dilation during phacoemulsification. *Philippine Journal of Ophthalmology* 2013; 2(1):12-18.
- Minj A, Satapathy J, Kumar A. The importance of preoperative topical non-steroidal antiinflammatory agents in cataract surgery- an open label prospective randomised comparative study. *Trop J Ophthalmol Otolaryngol*.2019; 4(5):334-340.
- Rodríguez-García A, Hernández-Camarena JC, López-Jaime GR, Nava-García JA. Effect of Topical Nonsteroidal Anti-inflammatory Drugs on Pupillary Size During Uncomplicated Cataract Surgery. *J Refract Surg*. 2017 Apr 1;33(4):236-242.

DATA SHARING STATEMENT: The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

CONFLICT OF INTEREST: Authors declared no conflict of interest.

GRANTED SUPPORT AND FINANCIAL DISCLOSURE: Nil

AUTHOR'S CONTRIBUTION

The following authors full fill authorship criteria as per ICMJE guidelines;

Salahuddin: Idea conception, drafting the work, Data analysis, final approval, agreed to be accountable for all the work.

Rashid H: Design of the work, data acquisition, Data interpretation, critical revision, final approval, agreed to be accountable for all the work.