



Original Article

Comparison Between Topical Nepafenac and Flurbiprofen in Maintaining Intraoperative Mydriasis and Controlling Postoperative Inflammation in Cataract Surgery.

Varsha V¹, Sandhya Ramachandra^{2*}, Sarala N³

1. Post Graduate, Department of Ophthalmology, Sri Devaraj Urs Medical College, Sri Devaraj Urs Academy of Higher Education and Research, Kolar.
2. Senior Consultant and DNB Professor, K C General Hospital, Malleswaram, Bangalore.
3. Professor and HOD, Department of Pharmacology, Sri Devaraj Urs Medical College, Sri Devaraj Urs Academy of Higher Education and Research, Kolar.

Abstract

Background: Preoperative dilation of pupil is one of the prerequisites to perform an uncomplicated cataract surgery. Intraoperative miosis is one of the many challenges which a surgeon can encounter during cataract surgery. Preoperative use of NSAIDS like nepafenac, flurbiprofen, ketorolac have been used for maintaining intra operative mydriasis and controlling postoperative inflammation by blocking prostaglandin synthesis.

Aims: To compare the efficacy of nepafenac and flurbiprofen in maintaining intraoperative mydriasis and controlling postoperative inflammation

Settings and Design: This was an institutional prospective comparative study done in rural Karnataka.

Methods and Material: This study was performed on 110 patients, 55 were allocated in each group and were given either of the topical NSAID's Nepafenac or Flurbiprofen prior to cataract surgery. Pupillary diameter was measured at the beginning and at the end of the surgery and the values were compared between the groups. Postoperative inflammation was also compared between both the groups.

Statistical analysis used: The difference in flare and cells grading across groups were tested using Chi-Square test. p value of < 0.05 was considered statistically significant

Results: The mean pupillary diameter of the two groups were comparable at the beginning of surgery. The mean change in the pupillary diameter was more in flurbiprofen group when compared to nepafenac group. There was statistically significant difference among both the groups in maintenance of intraoperative mydriasis. The comparison of postoperative inflammation was also statistically different between both the groups.

Conclusions: Pre-operative Nepafenac was found to be better than flurbiprofen in maintaining intraoperative mydriasis and controlling postoperative inflammation.

Keywords: Cataract surgery, Surgical miosis, NSAIDs, Nepafenac, Flurbiprofen.

*Corresponding Author

Dr. Sandhya Ramachandra

Senior Consultant and DNB Professor,
K C General Hospital, Malleswaram,
Bangalore-560003.

Mobile No: 9844177487

E-mail: sanchina@rediffmail.com

Conflict of Interest: None

Financial Aid: Nil

Introduction

Senile cataract is the leading cause of avoidable blindness throughout the world contributing to 39.1% of global blindness.¹ The definitive treatment of cataract is the surgical removal of the cataractous lens and replacement with an intraocular lens (IOL). Extracapsular Cataract Extraction (ECCE) with the implantation of an IOL became the preferred method of cataract surgery in the 1980s and today most surgeons in developing countries have been trained in

this technique. The use of a smaller incision with the advantages of faster rehabilitation, less astigmatism and better postoperative vision without spectacles led to phacoemulsification becoming the preferred technique where resources are available. However, cost, both in terms of equipment and training has limited its use in the developing world. Thus, Manual suture less Small Incision Cataract Surgery (SICS) has been the technique increasingly employed in developing countries. Manual SICS is comparable to phacoemulsification in achieving excellent visual outcomes with low complication rates, but is significantly faster, less expensive and requires less technology.

Maintaining the mydriasis is an essential prerequisite for uneventful cataract surgery. In Small Incision Cataract Surgery (SICS) all the manipulations are done in the posterior chamber (PC) of eye, the visibility of which is possible by pupillary dilatation (mydriasis).

Preoperative dilatation of pupil is usually achieved by cyclopentolate 1% eye drops or Tropicamide 0.8% with Phenylephrine 5% eye drops. However, inspite of adequate dilatation of pupil with mydriatics, intraoperative miosis is one of the challenges which a surgeon can encounter during cataract surgery leading to difficulty in performing precise anterior capsulorrhesis and safe phacoemulsification with IOL implantation, with high risk of posterior capsular rent, vitreous loss postoperative uveitis and cystoid macular edema.

Surgical trauma triggers the inflammatory cascade with release of Cyclooxygenase enzymes (COX-1 and COX-2) producing excessive quantities of prostaglandins in the anterior chamber, leading to miosis, inflammation and disruption of blood-aqueous barrier. Currently, two drug groups are available to control ocular inflammation: steroids and NSAIDs. Steroids are potent anti-inflammatory agents that work by acting on a number of intercellular inflammatory mediators. Long term usage of steroid is associated with increase in IOP .NSAIDs inhibit cyclooxygenase enzyme, thereby interfering with endogenous prostaglandin production, thus preventing intraoperative miosis and controlling postoperative inflammation.²

Non-Steroidal Anti-Inflammatory drugs (NSAIDs) like Nepafenac ,Flurbiprofen and Ketorolac are effective in maintaining intraoperative mydriasis and controlling postoperative inflammation.³

This study specifically intended to measure the horizontal and vertical pupillary diameters at the beginning and end of surgery to compare the total

loss and percentage total loss of mydriasis between flurbiprofen 0.03% and Nepafenac 0.1%.This study also compared the postoperative inflammation between both the groups.

Material and Methods

This Prospective comparative strudy will be conducted on 110 eyes of patients with senile cataract attending the department of Ophthalmology, R. L. Jalappa Hospital& Research centre, Kolar from December 2018 to June 2020. The study will be conducted after obtaining ethical clearance from Institutional Ethical Committee of Sri Devaraj Urs Medical College and written informed consent from the subjects.

Males and females aged 50 years and above with senile cataract undergoing Manual small incision cataract surgery with intraocular lens implantation were included in the study. Patients with systemic comorbidities like hypertension, diabetes. Ocular co morbidities Pseudoexfoliation, primary or secondary glaucomas, uveitis, history of ocular trauma or ocular surgery to the operating eye, Patients on topical or systemic steroids and NSAIDs within 30 days prior to inclusion in the study, history of hypersensitivity to nepafenac or flubiprofen, patients with pupil diameter less than 6 mm with mydriatic were excluded from the study.

The selected patients were randomized into two groups based on random number table prepared using random number generator in to two groups A and B.

GROUP A: 55 EYES- Nepafenac 0.1%

GROUP B: 55 EYES- Flurbiprofen 0.03%

Technique

Preoperative: All patients received oral tab Ciprofloxacin 500mg twice daily and Ciprofloxacin 0.3%eye drops hourly one day before the surgery. Group A received nepafenac 0.1% three times one day before surgery. One drop every 30 minutes was instilled just before the planned time of surgery. Group B received 0.03% of Flurbiprofen eye drops 3 times one day before surgery. One drop every 30 minutes was instilled just before the planned time of surgery .Both Group A and Group B received Tropicamide 0.8% with Phenylephrine 5% ophthalmic solution 2 times at an interval of 10 minutes, half an hour before surgery. The diameter of the pupil was measured in both horizontal and vertical meridian using Castroviejo's calipers before peribulbar anesthesia.

Intraoperative: All patients underwent small incision cataract surgery with posterior chamber IOL implantation under peribulbar anesthesia. During the procedure, the horizontal and vertical pupillary diameters were measured using Castroviejo's calipers during the following two steps of the surgery, i) After initial entry in to the anterior chamber , ii) After IOL implantation, upon completing the intervening surgical steps

Postoperative: Routine standard post operative protocol of ciprofloxacin and dexamethasone eye drops were given 6 times a days for the first week. It was then tapered over 5 weeks. On day 1 visual acuity was recorded and slit lamp examination was done for detailed assessment and documentation of post operative inflammation and graded according to Standard Uveitis Nomenclature (SUN Classification). The same was done day7.

Statistical Methods Used For This Study

Collected data were coded and entered in MS Excel and analysed using SPSS22 version software. Categorical variable like gender, eye(R/L) will be expressed using proportion(%). Continuous variables like age, mydriasis were expressed using mean \pm SD or median (IQR) depending on normal distribution. The difference in flare and cells grading across groups were tested using Chi-Square test. P value of < 0.05 was considered statistically significant

Results

There was equitable distribution of age between both groups Table1 and male

The average preoperative pupil diameters was comparable between the groups and there was no statistical significance. The difference in vertical and horizontal pupil diameters at the end of the

preponderance was found among the participants in the study Table 2

Table 1: Age distribution between both the groups.

Parameter	Group A (Nepfenac) (n=55)	Group B (Flubiprofen) (n=55)
Age (years) (Mean \pm SD)	63.27 \pm 7.86	62.87 \pm 8.38

Table 2: Gender distribution in both groups.

Parameter	Group A (Nepfenac) (n=55)	Group (Flubiprofen) (n=55)
Male	25(47%)	33(59%)
Female	29(53%)	23(41%)

Left Eye preponderance was observed only in the flurbiprofen group Table 3.

Table 3: Distribution of laterality in both the groups.

Parameter	Group A (Nepfenac) (n=55)	Group B (Flubiprofen) (n=55)
LE	27(49%)	35(64%)
RE	28(51%)	20(36%)

surgery in both the groups was found to be statistically significant. The percentage loss of both vertical and horizontal pupil diameters was more in group B when compared to group A Table 4 & 5.

Table 4: Comparison of vertical pupil diameters (mean \pm SD in mm) between both the groups at different stages of cataract surgery.

Parameter	Group A (Nepfenac)	Group B (Flubiprofen)	P value
Preoperatively	7.59 \pm 0.57	7.67 \pm 0.51	0.45
End of Surgery	6.98 \pm 0.79	6.34 \pm 1.07	0.00
Total Change	0.59 \pm 0.63	1.33 \pm 1.05	0.00
% Loss*	7.46	16.67	0.00

Table 5: Comparison of horizontal pupil diameters (mean ± in mm) between both the groups at different stages of cataract surgery

Parameter	Group A (Nepfenac)	Group B (Flubiprofen)	P value
Preoperatively	7.52±0.61	7.65±0.51	0.22
End of Surgery	6.80±1.25	6.34±1.07	0.04
Total Change	0.57±0.63	1.31±1.05	0.00
% Loss*	7.53	16.25	0.00

There was a significant difference in flare and cells between both the groups on day 1. On day 7 the inflammation between both the groups showed no statistical significance Table 6.

Table 6: Comparison of flare and cells of day 1 and 7 between both the groups.

	Group A (Nepfenac)	Group B (Flubiprofen)	P value
Post OP Day 1 Flare			0.02
0	36(65%)	24(43%)	
1	19(35%)	31(55%)	
2		1(2%)	
Post OP Day 7 Flare			
0	55(100%)	55(100%)	
Post OP Day 1 Cell			0.00
0	37(65%)	11(21%)	
1	18(35%)	44(79%)	
Post OP Day 7 Cell			
0	55(100%)	55(100%)	

There was no significant difference in postoperative BCVA between both the groups on Day 1 and Day 7.

Table 7: Comparison of BCVA between both the groups on day 1 and day 7

BCVA (LogMAR)	Group A (Nepfenac)	Group B (Flubiprofen)
BCVA POD 1		
0	49(89%)	48(87%)
0.3	6(10%)	7(13%)
BCVAPOD 7		
0	54(98%)	53(96%)
0.3	1(2%)	2(4%)

Discussion

Miosis due to surgical trauma is one of the most challenging obstacle that come in the way of a successful cataract surgery. It can lead to many intraoperative and postoperative complications like difficulty in nucleus delivery ,posterior capsular tear, vitreous loss, increased permeability of the blood-ocular barriers , postoperative inflammation and changes in intraocular pressure

Topical Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) are important topical drugs that assist cataract surgeons to reduce intraoperative miosis, and are beneficial in controlling postoperative pain and inflammation.

In our study , the preoperative use of flurbiprofen and nepafenac for maintenance of intraoperative mydriasis and controlling postoperative inflammation in cataract surgery was studied.

Assessment of Pupil diameters

The vertical and horizontal pupil diameters were comparable between both the groups preoperatively. At the end of the surgery however ,the percentage loss of mydriasis was less in nepafenac group.

This was comparable to a study by Sarkar et al where the total reduction in vertical pupillary diameter from the beginning to the end of surgery was significantly less in nepafenac group.⁴

Rodríguez-García A et al compared the effectiveness of 0.1% nepafenac, 0.03% flurbiprofen, 0.4% ketorolac and control group in inhibiting surgically induced miosis during uncomplicated cataract surgery. The percentage of pupillary area loss at the end of surgery was less in nepafenac group.

Intraocular drug concentrations are an important determinant of the anti-inflammatory efficacy of a drug. The near maximum concentration of amfenac is maintained longer. That may explain the prolonged duration of action of nepafenac relative to other drugs in this class.⁵

The results of our study was not consistent with The present study differed from the findings of Prakash et al, where both nepafenac and flurbiprofen were efficient in maintaining intraoperative mydriasis.⁶

Assessment of Postoperative inflammation

The study found that Postoperative inflammation, assessed by flare and cells, was better controlled by nepafenac than flurbiprofen on postoperative day 1. However on day 7, postoperative inflammation was comparable between both the groups.

In a study by Lane.S.S et al it was found that nepafenac 0.1% was better than placebo in controlling post operative inflammation.⁷A study by Hebbar et al showed that both the medications, topical bromfenac 0.09% and topical flurbiprofen 0.03% effective and safe in reducing pain and anterior chamber inflammation after cataract surgery but the response was earlier with bromfenac 0.09%.⁸

Walters et al. found that nepafenac has better bioavailability and Cmax achievement. This may be the cause of slight early better results observed with nepafenac over the anterior chamber cells and flare with respect to flurbiprofen in our study.⁹

Multicentric randomized studies are required to assess the exclusive safety and efficacy of NSAIDs on postoperative inflammation which if proven can substitute the steroids. This study has taken into consideration only uncomplicated cataract surgery. Also the comparative efficacy of the these drugs in diabetics and eyes with ocular inflammation needs to be studied.

In this study Nepafenac was found to be better than flurbiprofen in maintaining mydriasis intraoperatively and controlling postoperative inflammation.

References

1. Murthy. GVS. Blindness: An International Perspective. In: Chaudhuri Z, Vanathi M(Eds) Postgraduate Ophthalmology,1sted. New Delhi: Jaypee highlights Medical Publishers;2012:p. 3-17.
2. Suleiman YM, Krdoghli NF, Ahmad AJ. Comparison of Ketorolac Tromethamine and Prednisolone Acetate in Preventing Surgically Induced Miosis during Cataract Surgery. Sultan Qaboos Univ Med J 2010;10(1):57-63.
3. Sharma AK, Sharma HR, Sharma R, Singh A. Comparison of preoperative Dexamethasone Phosphate versus Ketorolac Tromethamine in maintaining Intraoperative mydriasis during Small Incision Cataract Surgery. J Clin Diagn Res 2016;10 (5):9-13.
4. Sarkar S, Mondal KK, Roy SS, Gayen S, Ghosh A, De RR. 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 J Pharmacol 2015;47 (5):491-5.
5. 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;33(4):236-42.

6. Prakash S, Basavaraj Bhandare SV, Kumar K. A comparative study on efficacy of nepafenac and flurbiprofen in maintenance of intraoperative mydriasis during cataract surgery: an openlabel randomized controlled trial. IJBCP 2018 ;7(4):617.
7. Lane SS, Modi SS, Lehmann RP, Holland EJ. Nepafenac ophthalmic suspension 0.1% for the prevention and treatment of ocular inflammation associated with cataract surgery. J Cataract Refract Surg 2007;33(1):53-8.
8. Hebbar SK, Deepak P, Nalini GK, Kavitha CV, Sahana GN, Nagaral JV. A prospective evaluation of efficacy and safety of topical bromfenac 0.09% over topical flurbiprofen 0.03% after cataract surgery. IJBCP 2019;8(2):234.
9. Walters T, Raizman M, Ernest P, Gayton J, Lehmann R. In vivo pharmacokinetics and in vitro pharmacodynamics of nepafenac, amfenac, ketorolac, and bromfenac. J Cataract Refract Surg 2007;33(9):1539 -45.