Original Article

Efficacy of Nepafenac 0.1% in Maintaining Mydriasis during Phacoemulsification Surgery

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ABSTRACT

OBJECTIVE: To determine the efficacy of Nepafenac 0.1% eye drops in maintaining mydriasis during phacoemulsification cataract surgery.

METHODS: Patients of 40 – 65 years of age undergoing phacoemulsificaton cataract surgery were randomly divided into two groups. One group received Nepafenac 0.1% eye drops and the other group received placebo (Tears Naturale II eye drops).

Pre – operatively; all patients received tropicamide 1% eye drops and phenylephrine 2.5% eye drops. The surgery in all the cases was done by the same ophthalmologist; with intra – operative epinephrine in the irrigating solution. The pupil size was measured with caliper at three steps; immediately before the surgical incision (baseline), at the end of phacoemulsification, and at the end of surgery.

RESULTS: 60 eyes of 60 patients were included in the study. 30 eyes were in the Nepafenac 0.1% group and another 30 in the placebo group. The mean age of our patients was 54.18 ± 7.49 years. 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 group (P– Value < 0.001).

In the Nepafenac group; the pupil size at the end of surgery decreased by a mean of 0.55 ± 0.51 mm (range 0.00 – 1.50 mm). Meanwhile; in placebo group the pupil size decreased by a mean of 1.05 ± 0.87 mm (range 0.00 – 3.5 mm). This difference was statistically significant (P = 0.009).

CONCLUSION: The pre – operative use of Nepafenac 0.1% eye drops was effective in maintaining mydriasis during phacoemulsification cataract surgery.

KEY WORDS: Cataract, mydriasis, Nepafenac.

INTRODUCTION

The standard surgical procedure for cataract surgery nowadays is phacoemulsification with intraocular lens (IOL) implantation; that gives the excellent visual results. Stable and adequate mydriasis is required throughout phacoemulsification operation. Constriction of the pupil (miosis) during phacoemulsification cataract surgery can lead to posterior capsule rupture and loss of nucleus.[1]

The pre – operative topical use of anticholinergics (i.e. tropicamide 1%) and sympathomimetics (i.e. phenylephrine 2.5%) provides adequate pupil dilatation before surgery. Also; intra – operative adrenaline in the irrigation solution is being used to maintain mydriasis during cataract surgery.[2]

During cataract surgery surgical trauma to the anterior segment may cause breakdown of blood aqueous barrier resulting in constriction of the pupil (miosis) due to release of prostaglandins (PGs). The non – steroidal anti – inflammatory drugs (NSAIDs) cause Cyclo – Oxygenase (COX) enzyme inhibition and thereby; inhibit the production of prostaglandins.[3]

Indomethacin in 1983 was the first topical ophthalmic NSAID used; to reduce the pupillary constriction that occurs during cataract extraction surgery. Topical flurbiprofen 0.03 % (in 1987) and suprofen 1% (in 1989) had been approved by FDA (Food and Drug Administration) of USA for inhibiting intra – operative miosis.[4, 5] The NSAIDs causes punctate epithelial erosions; and rarely corneal melting and ulceration may occur.[6]

Since a long time; the research is going on for a better NSAID with less side effects. Various studies have shown that topical ketorolac tromethamine 0.5 % and diclofenac sodium 0.1% are effective as flurbiprofen in inhibiting intra – operative miosis.[7] Also; ketorolac tromethamine 0.4% is reported to be effective in maintaining mydriasis during cataract surgery.[8]

FDA in August 2005 has approved new ophthalmic suspension Nepafenac 0.1% (Nevanac ®); as a therapy of inflammation and pain occurring during cataract surgery. Nepafenac 0.1% is a unique NSAID; because it is a pro drug which rapidly penetrates the cornea and is hydrolyzed to the active metabolite Amfenac; by enzymes present in iris, ciliary body, retina & choroid. Amfenac is a non – selective COX enzyme inhibitor that blocks the synthesis of PGs.[9, 10]

The diffusion of Nepafenac to the anterior and posterior segments of the eye is augmented due to its Pro drug structure. It also reduces the hazard of toxicity on

the corneal surface. [11] The aim of this study was to evaluate the mydriasis – maintaining effect of pre – operative Nepafenac 0.1% eye drops during phacoemulsification surgery and thereby; we can prevent per – operative complications (i.e. posterior capsule rent and nucleus drop) which commonly occur if the pupil constrict during surgery.

MATERIAL AND METHODS

This cross sectional study was carried out from 1st September 2010 to 31st August 2011; at a tertiary care eye centre in Hyderabad.

Patients of 40 – 65 years of age with cataract undergoing phacoemulsification surgery were studied. Patients with pseudoexfoliation, or local pupil abnormalities such as posterior synechiae, ocular trauma or previous intraocular surgery and diabetes mellitus, were excluded.

After taking written informed consent from the patients; they were randomly divided into two equal groups. One group received Nepafenac eye drops (4 drops; 1 drop at 15 minutes interval beginning 1 hour before surgery), and the other group received placebo (Tears Naturale II) eye drops. The surgeon was masked to patient randomization.

The pupil was dilated in all the patients with topical tropicamide 1% and phenylephrine 2.5% eye drops (4 drops; 1 drop every 15 minutes beginning 1 hour before surgery). The surgery was performed in all the patients with intra – operative epinephrine in the irrigating solution.

The diameter of pupil as viewed through the operating microscope was measured with caliper at three steps; immediately before the surgical incision (baseline), at the end of phacoemulsification and at the end of surgery. Eyes with < 7.0 mm pupil size at the baseline; or with eventful surgery (i.e. vitreous loss) were excluded from the study.

We calculated the sample size based on a study conducted on a rabbit model.[12] In that study; the mean pupil diameter in Nepafenac group was 11.5 ± 0.5 mm V/s 10.2 ± 1.1 mm in control group. So; we used the openepi software to calculate the sample size for our study by comparing the two means. With Confidence Interval at 95% & Power at 95%; the estimated sample size was 30 eyes in each group.

The data entered and analyzed on SPSS version 11. The mean age of patients and the frequency & percentages regarding their gender were calculated. The mean diameter of pupil measured at various surgical steps (at baseline, at end of phacoemulsification and at end of surgery) was calculated. Also; the mean decrease in pupil size from baseline to end of surgery was calculated and compared between the Nepafenac group and the Placebo group. The significance of difference in the mean pupil size between the two groups was determined using the ANOVA test. P – Value <0.05 was taken as significant.

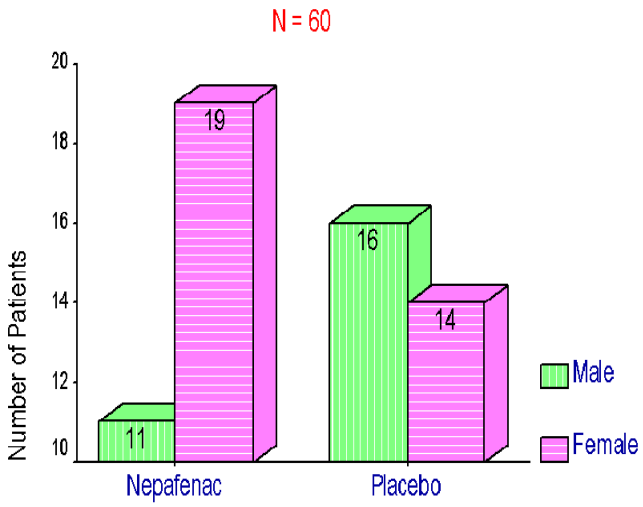
RESULTS

In this study 60 eyes of 60 patients were included. 30 were in the Nepafenac 0.1% group and another 30 in placebo group. 33 patients were females and 27 were males. The male: female ratio was 1:1.2 (**Figure I**). The age of our patients ranged from 40 – 65 years. The mean age of our patients was 54.18 ± 7.49 years. The mean age of patients in Nepafenac group was 55.47 ± 6.56 years V/s 52.90 ± 8.24 years in the Placebo group. This difference was statistically insignificant (P = 0.187).

The ANOVA test revealed; a statistically significant difference of mean pupil size measured at different steps of surgery between the Nepafenac and Placebo groups (P – Value ≤ 0.001) (**Figure II**). The mean diameter of pupil at end of Phaco was 8.0 ± 0.54 mm in Nepafenac group V/s 6.98 ± 0.72 mm in placebo group. Meanwhile; the mean diameter of pupil at the end of surgery was 7.65 ± 0.71 mm in Nepafenac group V/s 6.67 ± 0.97 mm in placebo group (**Table I**).

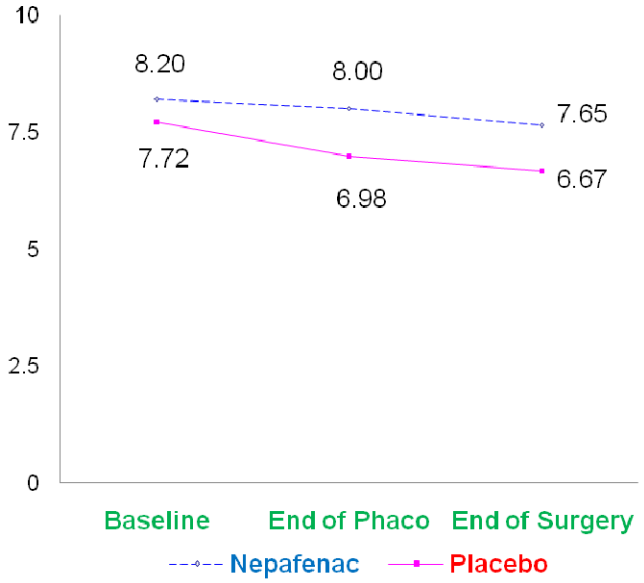
The mean decrease in pupil size from baseline to end of Phaco was 0.20 ± 0.31 mm (range 0.00 – 1.00 mm) in Nepafenac group V/s 0.73 ± 0.60 mm (range 0.00 – 3.0 mm) in placebo group (P – Value < 0.001) (**Figure III**). Meanwhile; the mean decrease in pupil size from baseline to the end of surgery was 0.55 ± 0.51 mm (range 0.00 – 1.50 mm) in Nepafenac group V/s 1.05 ± 0.87 mm (range 0.00 – 3.5 mm) in placebo group (P = 0.009) (**Figure IV**).

Figure - 1



Gender between the two drug groups

FIGURE II: (n=60)



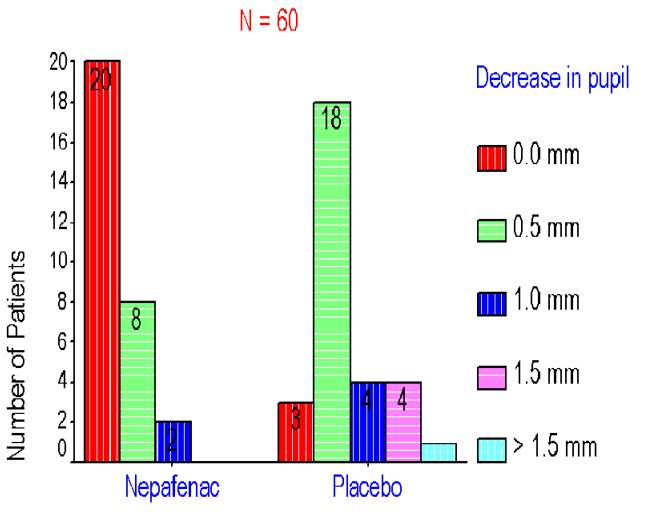
Trend of mean pupil size at different steps of surgery

TABLE I: COMPARISON OF MEAN ± STANDARD DEVIATION OF PUPIL SIZE (IN MM) AT DIFFERENT STEPS OF SURGERY (n=60)

Pupil Size	Nepafenac n = 30	Placebo n = 30	P-Value †
Baseline	8.20 ± 0.50	7.72 ± 0.52	0.001 *
End of Phaco	8.00 ± 0.54	6.98 ± 0.72	< 0.001 *
End of Surgery	7.65 ± 0.71	6.67 ± 0.97	< 0.001 *

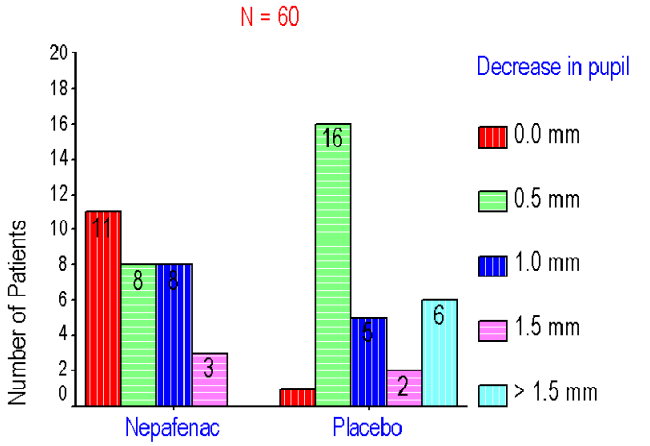
† By ANOVA test, * Significant difference

Figure - 3



Decrease in Pupil Size from baseline to End of Phaco

Figure - 4



Decrease in Pupil Size from baseline to End of Surger

DISCUSSION

Recently topical ophthalmic NSAIDs are used in cataract surgery for prevention of intra operative miosis, treatment of post operative inflammation and for prevention and treatment of cystoid macular edema (CME).[13, 14]

Riaz N in his study conducted at Lahore had reported that; diclofenac sodium 0.1% was helpful in retaining mydriasis during phacoemulsification surgery [15]. The mean decrease in pupil size from baseline to the end of surgery was 0.9 mm in placebo group V/s 0.4 mm in diclofenac group. The results of Riaz N [15] were similar to our study; where the decrease in pupil size in placebo group was almost twice the decrease in pupil size in Nepafenac group.

Similarly; Cervantes-Coste et al [16] from Mexico had reported that; the pre operative use of nepafenac 0.1% was helpful in retaining mydriasis during phacoemulsification surgery. The reduction in pupil diameter from beginning to the end of surgery was 1.59 ± 0.94 mm in control group V/s 0.78 ± 0.56 mm in nepafenac group.

Since many years; intra – operative 1:1000 adrenaline in the irrigating solution is being used intracamerally to maintain mydriasis during cataract surgery. Mydriasis can be also be maintained with one bolus of dilute epinephrine (0.1 ml of 1:25,000) intracameral injection during surgery.[17]

Altaf et al [18] in a study conducted at Rawalpindi on patients undergoing extra capsular cataract extraction (ECCE) surgery had reported that; the group receiving topical flurbiprofen 0.03% along with per – operative epinephrine showed better maintenance of mydriasis than the group treated with epinephrine alone. This

additive effect on the maintenance of mydriasis; when both intra – operative adrenaline and pre – operative topical NSAIDs were used together has been demonstrated in various studies. [3, 5, 7 and 19]

Ong-Tone and Bell [20] from Canada had conducted a study to determine whether adrenaline in the irrigating solution is necessary when diclofenac eye drops are used before phacoemulsification surgery. All of the 207 patients used diclofenac eye drops two days pre – operatively; and then they were divided into 2 groups. One group received 0.5 ml of 1:1000 adrenaline in 500 ml of balanced salt solution (adrenaline group), and the other group did not (No – adrenaline group).

At the end of surgery; the mean pupil constriction was 0.05 ± 0.21 mm in the adrenaline group V/s 0.33 ± 0.43 mm in No – adrenaline group. Ong-Tone and Bell [20] had concluded that; adrenaline in the irrigating solution does not appear necessary when diclofenac eye drops are used before phacoemulsification surgery; especially in eyes with large pre – operative pupils (8 mm at the baseline).

RECOMMENDATIONS

We recommend the use of Nepafenac 0.1% eye drops pre – operatively to maintain mydriasis during phacoemulsification cataract surgery, and thereby; making the surgery easier and safer.

CONCLUSION

Our study has confirmed that; the use of Nepafenac 0.1% eye drops along with conventional mydriatics (pre-operative tropicamide 1% eye drops and phenylephrine 2.5% eye drops along with intra – operative 1:1000 adrenaline in the irrigating solution) is effective compared to conventional mydriatics alone; in maintaining the pupil dilated during the phacoemulsification surgery.

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