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A COMPARATIVE TRIAL TO STUDY THE EFFICACY OF TOPICAL NSAID'S (NEPAFENAC, BROMFENAC AND FLURBIPROFEN) IN MAINTAINING THE INTRAOPERATIVE MYDRIASIS DURING CATARACT SURGERY

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ABSTRACT **AIM –** To assess and compare the role of topical nepafenac (0.1%) , flurbiprofen (0.03%) and bromfenac (0.09%) in sustaining intra-operative mydriasis while doing cataract surgery. **STUDY DESIGN –** Observational prospective randomised study **METHOD** - Study was done on 150 patients having age 30-80 years, planned for cataract surgery with PCIOL implantation. Topical NSAIDs (nepafenac {A} , flurbiprofen{B} and bromfenac{C}) were administered to the cataract patients before cataract surgery. Horizontal pupillary diameter were measured at four steps under operating microscope ; immediately before the surgical incision (baseline) , just after capsulorhexis, after nucleus delivery and at the end of irrigation and aspiration ; average values were calculated for the three groups. **RESULT -** Horizontal pupillary diameter at STEP 0 , I,II and III, was more in nepafenac and least in flurbiprofen and the difference was statistically significant between 3 groups ($p<0.001$). Mydriasis sustaining effect was more pronounced in groups A and C than in group B. **CONCLUSION-** In the present study , both nepafenac (0.1%) and bromfenac (0.09%) administered before operation are helpful in sustaining pupil size intra-operatively during SICS/Phaco.

KEYWORDS : nepafenac, flurbiprofen, bromfenac intra-operative mydriasis.

INTRODUCTION

Pupillary dilatation plays a pivotal role in the success of cataract surgery, making it an essential step in preoperative preparation. The ease of doing cataract surgery largely depends on the view governed by pupillary dilatation. Controlling pupil dynamics is very important during surgery, so one should be aware of the risk factors to effectively anticipate and address intraoperative miosis. Adequate and stable mydriasis is a pre-requisite for quick and safe cataract surgery. Cataract surgery needs proper visualization, especially phacoemulsification, which is performed through small clear corneal incision.

Every step is crucial and each step can worsen upcoming steps .It is very difficult to make an appropriately sized capsulorhexis in the setting of an inadequate mydriasis. Incomplete rhexis is always at high risk of extension, leading to lens or intraocular lens drop in the later part of the surgery. Because of a compromised surgical field for phacoemulsification, iris can be injured with a phaco – probe, which will further instigate iris movements and bellowing. A trauma to the iris vessels can lead to hyphaema, which further limits visibility. Any iris defect that occurs during surgery can lead to significant visual complaints post-operatively like uniocular diplopia, glare.

A study by Guzek et al revealed that there is a fifty percent reduction in incidence of posterior capsule rupture if pupillary diameter is maintained above 6 mm throughout the surgery and each 1 mm reduction in pupil size doubles the risk of complications.[1] Also, intraoperative miosis (<6 mm) results in an increase in other complications such as lens decentration , retained lens fragments, postoperative inflammation and vitreous loss.[1–6]

Because of difficulties induced by intraoperative miosis and manoeuvres to dilate the pupil, the total duration of surgery increases, increasing intraocular inflammation and intraocular pressure.

Surgical trauma in manipulation and other types of stimulation of ocular structure elicits complex reaction including miosis, ocular hypertension, breakdown of blood aqueous barrier and vasodilatation. These events occur by intraoperative release of prostglandins and by the chemical mediators such as substance P.

There are several neurotransmitters including acetylcholine, histamine, leukotrienes, vasoactive intestinal polypeptides and other neuropeptides that must be considered as a mediator of surgical induced miosis. Of these, acetylcholine is a universal mediator. However a surgical procedure involving excessive trauma may also cause the release of intra-cellular enzymes and other cytoplasmic substances and ions in addition to autocoids and neurotransmitters.

Nonsteroidal anti-inflammatory drugs have been attempted to eliminate the problem of miosis secondary to the actions of prostaglandins and others as yet unknown chemical mediators liberated during cataract surgery.

NSAIDs act as cyclooxygenase (COX) inhibitors. COX enzyme is responsible for synthesis of prostaglandins. Prostaglandin secretion is induced by intraocular manipulation, which further induced intraoperative miosis. Thus, NSAIDs cause inhibition of prostaglandin synthesis by inhibiting COX and prevent intraoperative miosis [7,8].

NSAIDs were the first FDA approved drug to be used for preventing intraoperative miosis .Multiple NSAIDs are proven to be effective in avoiding intraoperative miosis, with flurbiprofen being the first one to be approved. Other drugs are diclofenac, ketorolac, bromfenac, nepafenac. This drug when instilled topically in eye, reduces miosis and prevents disruption of blood aqueous barrier and works as an anti-inflammatory without altering intraocular pressure.

MATERIALS AND METHODS

This is a prospective comparative observational randomized study done in ophthalmology department after taking approval from the Institutional Ethical Committee. One hundred and fifty eyes of 150 patients with senile cataract were included. Written and informed consent was taken from all the participants. Patients with glaucoma, uveitis, ocular surface disorders, history of any ocular surgery or trauma in operating eye, allergy or hypersensitivity to the preservatives or topical NSAIDs or any other component of study medication, were excluded.

This study comprised of 150 patients, who were divided into three groups of 50 each (group A, B and C) after randomisation . Patients in group A received Nepafenac (0.1%) while those in group B received Flurbiprofen (0.03%) eye drops and group C received bromfenac (0.09%), which was provided after removing labels, wrapping them with white paper and coding them as A ,B and C . A designated resident who was not involved in the study was assigned the work of enrolling participants and putting eye drops. The operating surgeon and the patients undergoing surgery were unaware of the type of drug administered. A thorough ophthalmic examination including best-corrected visual acuity (BCVA) using Snellen's chart, anterior segment evaluation by slit lamp bio-microscopy, intraocular pressure measurement by Goldmann applanation tonometry, dilated fundus

examination by indirect ophthalmoscopy ,grading of cataract was done for all subjects included in the study. Medical, surgical history and use of any current medications were extensively reviewed.

Pre-operatively, all patients received one drop of tropicamide 0.8% and phenylephrine 5% (combination), 4 times, at an interval of 15 minutes on the day of surgery. Thereafter, Nepafenac drop in group A/Flurbiprofen drop in group B / Bromfenac drop in group C was administered 4 times, at an interval of 15 minutes keeping a gap of 10 minutes between tropicamide-phenylephrine and any of the experimental drugs.

In all the groups, surgery was done in same way by one ophthalmic surgeon. Calliper was used to measure pupillary diameter at four steps under operating microscope ; immediately before the surgical incision (baseline) , just after capsulorhexis (STEP I), after nucleus delivery(STEP II) and at the end of irrigation and aspiration (STEP III). Pupillary diameter measurement values were described as percentage, mean and standard deviation. Chi-square test , ANOVA test was used for analysing categorical variables and unpaired two tailed t-test was used for continuous variables. A P value of less than 0.05 was considered statistically significant. All analysis was performed using SPSS software(version 11.5 ; SPSS Inc, Chicago, IL)

RESULT

In the study, 150 patients were selected, 50 patients to be chosen randomly for each group. No statistically significant differences were present between the three groups. The mean age of patients was 60.2 +_ 10.7 years; 75.5% being females. There was no significant difference in age, gender and laterality of eye between the two groups.
It was found that there was less reduction in size of pupil in nepafenac and bromfenac group than flurbiprofen group. Overall there was 2.02 mm average decrease in pupillary diameter with nepafenac group , 2.00mm average decrease in pupillary diameter with bromfenac group and 2.42 mm average decrease in pupillary diameter in flurbiprofen group.

Nepafenac and bromfenac are significantly more effective than flurbiprofen in maintaining mydriasis during uncomplicated SICS and phacoemulsification surgery.

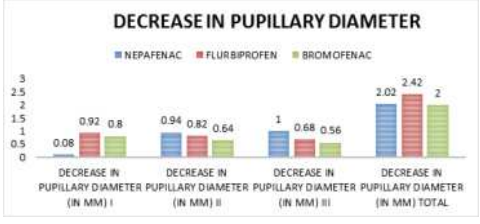

TABLE -1- shows decrease in pupillary diameter of all three drugs and was more in flurbiprofen and least in bromofenac and nepafenac.

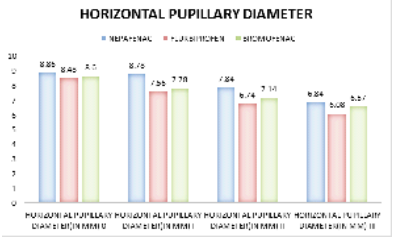

TABLE-2 shows horizontal pupillary diameter at STEP 0 , I , II and III , of all the three drugs used.

150 patients were included for final analysis of inflammatory response to treatment with nepafenac , bromfenac and flurbiprofen 50 patients in each group. Data was analysed on day 1, 7, 14 after surgery for conjunctival congestion , aqueous cells , corneal edema . The conjunctival congestion showed no statistically significant difference between three groups. The corneal edema showed no statistically significant difference between three groups.The aqueous cells showed no statistically significant difference between three groups.

The study demonstrate that all the three NSAIDs (nepafenac, bromfenac, flurbiprofen) are equally effective in reducing conjunctival congestion , corneal edema and aqueous cells.

In our study consisting of 150 patients of cataract, 50 in each group (nepafenac, bromfenac and flurbiprofen) no adverse reaction was observed.

DISCUSSION

It was found that there was less reduction in size of pupil in nepafenac and bromfenac group than flurbiprofen group. Overall there was 2.02 mm average decrease in pupillary diameter with nepafenac group , 2.00mm average decrease in pupillary diameter with bromfenac group and 2.42 mm average decrease in pupillary diameter in flurbiprofen group.

There was a significant decrease (22%) in pupil diameter at the end of the surgery in group B who were given flurbiprofen eyedrop prior to the surgery, as opposed to a small decrease observed in Groups A (6%) and C (5%) who received nepafenac and bromfenac respectively.

Difference between groups A and B, and groups A and C, was significant ($p<0.001$).

Nepafenac and bromfenac are significantly more effective than flurbiprofen in maintaining mydriasis during uncomplicated SICS and phacoemulsification surgery.

Psilas et al[9] compared indomethacin(1%), diclofenac (0.1%) and flurbiprofen (0.03%) with control group and measured pupil diameter at baseline, after capsulotomy, after expression of lens, after irrigation and aspiration of cortical remnants and found less pupillary constriction at baseline and after expression of the lens in indomethacin and flurbiprofen groups vs. control ($p=0.01$); less constriction at baseline and after irrigation or cortical remnants in indomethacin and flurbiprofen groups vs. control and diclofenac group ($p=0.001$). Indomethacin and flurbiprofen were more effective at maintaining mydriasis during cataract surgery than control or diclofenac.

Thus it shows that NSAIDs have a definite role in preventing intraoperative miosis. In NSAIDs (nepafenac, bromfenac and flurbiprofen) nepafenac and bromfenac comes out to be a far more better option flurbiprofen.

The study demonstrate that all the three NSAIDs (nepafenac, bromfenac, flurbiprofen) are equally effective in reducing conjunctival congestion , corneal edema and aqueous cells.

Bromfenac ophthalmic solution 0.09% is the first and only USA FDA-approved once daily ophthalmic NSAID for the treatment of postoperative ocular inflammation and reduction of ocular pain in patients who have undergone cataract extraction with posterior chamber IOL Implantation[10].

A prospective, open-label pilot study by Geneva and Henderson [11] evaluated the effectiveness of postoperative bromfenac 0.07% combined with loteprednol etabonate gel 0.5% for preventing macular thickening following phacoemulsification. The mean change in macular thickness at 3 to 4 weeks after surgery was small (1.26 µm, range -11 to +5 µm), suggesting that the combination of bromfenac 0.07% with a topical corticosteroid regimen may effectively minimize macular thickening following cataract surgery.

CONCLUSION

NSAIDs maintains pupillary diameter preoperatively. NSAIDs have a definite role in preventing intraoperative miosis. In NSAIDs, bromfenac and nepafenac are better than flurbiprofen in maintaining mydriasis preoperatively and intraoperatively. Nepafenac, bromfenac and flurbiprofen are equally effective in reducing conjunctival congestion, corneal edema and aqueous cells. No adverse reactions were observed in all three groups.

Thus to conclude, considering its potency in maintaining intraoperative mydriasis and other postoperative uses, we recommend topical Nepafenac (0.1%) as a potential choice to maintain intraoperative mydriasis during routine cataract surgery .

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