Study on efficacy of preoperative use of Flurbiprofen and Nepafenac eye drops in maintaining mydriasis during cataract surgery in comparison with duration of surgery in patients with senile cataract: A prospective randomized study.

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Abstract

Objective: Cataract surgery is the predominant procedure in day to day practice for many ophthalmologists. Maintaining appropriate mydriasis during surgery is the key for successful and safe surgery. Cataract surgery initiates the inflammatory cascade, thereby releasing prostaglandins. Prostaglandins lead to constriction of pupil during surgery. Topical NSAIDS are potent inhibitors of cyclooxygenase enzymes thereby inhibiting the biosynthesis of prostaglandins. Aim of the study is to compare the effectiveness of preoperative use of topical Nepafenac 0.1% and Flurbiprofen 0.03% eye drops in sustaining the mydriasis during surgery and comparison of efficacy of both in correlation with the duration of surgery.

Methods: We performed a Prospective, randomized, double blind, comparative study on 100 patients. Patients were randomly allocated into 2 equal groups to receive either Nepafenac or Flurbiprofen. Drug was allocated on the same day and prior to small incision cataract surgery. Pupil diameter was measured at the beginning and at the end of surgery and also duration of surgery was noted. The values of pupil diameter of both groups were compared and also with duration of surgery.

Results: A total of 100 eyes of cataract surgery patients, 46 males and 54 females with mean age group of 62.04 were included in the study. The mean horizontal (p-value=0.404) and vertical (p-value=0.279) diameter of Nepafenac and Flurbiprofen groups were almost similar with no statistically significant difference at the beginning and end of the surgery. There is not a statistically significant difference in variance of mean difference in pupil diameter among different time intervals. But there is a statistically significant difference in variance in mean deviation among patients in Nepafenac group (p-value=0.0089).

Conclusion: Topical Nepafenac and Flurbiprofen are equally effective in maintaining mydriasis, but Nepafenac is more efficacious in maintaining mydriasis as the duration of surgery is increased.

Keywords: Intraoperative, Intraocular lens, Blindness, Surgery.

Introduction

Cataract is the major cause of avoidable blindness worldwide, accountable for 47.8% of blindness, over 17.7 million blind people [1]. In India, cataract is responsible for 50%-80% of bilateral blindness [2]. Annually 3.8 million people become blind because of cataract in India [3]. After all, cataract is the most common cause of blindness, cataract surgery has become the prime concern in the global initiative-VISION 2020 “The Right to Sight” which is dedicated to eliminate avoidable blindness, by increasing the cataract surgery rate and its quality to attain good visual outcomes and enhance the quality of life by year 2020 [3]. Inspite of advances in cataract surgery such as Phacoemulsification has become the preferred technique in developed countries however small incision cataract surgery still remains as a preferred method in developing countries where cataract accounts for majority of the blindness [4].

During cataract surgery, intraocular tissue injury leads to activation of Phospholipase A2 and causes release of inflammatory mediators such as Prostaglandins and Leukotrienes. These endogenous prostaglandins induce miosis during surgery, increased permeability of blood aqueous barrier, conjunctival hyperemia, postoperative inflammation and intraocular pressure changes [5].

The reduction in pupil diameter can lead to more difficult surgery and the risk of surgical trauma, posterior capsule tear and postoperative inflammation is also increased. A study report showed that mydriasis larger than 6 mm during surgery has lessened the incidence of posterior capsule tear by half. Therefore, to ensure a safe cataract surgery, maintaining
an adequate mydriasis is considered important [6]. Topical ophthalmic NSAIDS play a major role in decreasing the release of prostaglandins by inhibiting cyclooxygenase enzyme [7]. Flurbiprofen is the first drug approved by FDA in 1988 used for maintaining intraoperative mydriasis [8]. Earlier studies have mentioned the efficacy of various topical NSAIDS in maintaining mydriasis during cataract surgery.

Newer topical NSAIDS like Nepafenac also showed promising effects. It is a prodrug, which inhibits cyclooxygenase enzyme. It has better corneal penetration and higher ocular bioavailability, resulting in target specific NSAID for prostaglandin inhibition [9]. Not many studies have been conducted in India comparing Flurbiprofen and Nepafenac. This is an efficacy study comparing topical Nepafenac and Flurbiprofen in maintaining mydriasis during cataract surgery in relation to duration of surgery.

Materials and Methods
The study is a randomized, prospective, double blind, single centre, longitudinal and comparative study conducted in patients undergoing small incision cataract surgery at a tertiary care hospital, South India. Approval of the ethics committee of the institution was taken. The study was conducted from August 2020 to December 2020. 100 patients who met the inclusion and exclusion criteria were taken as the sample size.

Inclusion criteria
- Patients age ≥ 50
- Patients diagnosed with senile cataract (irrespective of grade of cataract)
- Patients who underwent small incision cataract surgery with IOL implantation

Exclusion criteria
- Age <50 years
- History of trauma or any previous ocular surgeries in the operating eye
- Glaucoma or active ocular inflammation
- Ocular surface disease and viral keratoconjunctivitis
- History of diabetes mellitus and hypertension
- Use of topical or systemic steroids within 30 days prior to surgery.
- Use of any other topical medications within 30 days prior to surgery (except lubricants)
- Allergy or hypersensitivity to topical NSAIDS and its preservatives
- Intraoperative complications like iridodialysis, PCR, vitreous loss, premature entry or hyphema.

The study details were thoroughly explained to the patients and their relatives and informed consent was taken.

Thorough ophthalmic evaluation was done prior to surgery in all patients and proper history was taken especially medications regarding Benign prostrate hypertrophy as they cause floppy iris. Best corrected visual acuity using Snellen's chart, slit lamp biomicroscopy, IOP by non-contact tonometry, and dilated fundus examination was done. Cataract surgery consent was obtained from all patients. All the patients who met the inclusion criteria were randomly allotted in the two groups A and B with 56 patients in group A and 44 patients in group B.

Group A received 0.1% Nepafenac eye drops and group B received 0.03% Flurbiprofen eye drops. Patients in each group received drops 1 hour prior to surgery with one drop every 15 mins intervals and the last drop being administered 5 mins before peribulbar block. Mydriatic combination of tropicamide 0.8% and phenylephrine 5% was administered 1 hour prior to surgery with 15 mins interval, last drop was installed 10 mins before giving block in all the patients. There was a 5 mins gap during installation of two drops.

All the patients received moxifloxacin 0.5% eye drops 2 days prior to surgery and two times on the day of surgery. All patients underwent small incision cataract surgery with intraocular lens implantation under peribulbar anesthesia using lidocaine 2%, bupivacaine 5%, adrenaline 1 in 10,000 and sodium hyaluronidase. The horizontal and vertical pupil diameter measurements were taken before entry into anterior chamber and at the end of surgery. The measurements of all patients were taken using castroviejo’s callipers placed in front of the cornea, under the same microscope, using the same magnification by different surgeons. The duration of surgery was noted.

The other data collected were age, gender, laterality of eye being operated and the group of drops which they were receiving. The collected data was analyzed using SPSS version 20. Significance is assessed as p<0.05 and a linear regression analysis was done. Student t test has been used to find out the significance of study parameters on a continuous scale between two groups.

Results
Total 100 patients were included in the study. Patients were randomly allocated in each group with 56 in group A and 44 in group B. Table 1 shows the demographic profile of the two groups. There was no statistically significant difference in age, gender and laterality of eye in the two groups.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Nepafenac</th>
<th>Flurbiprofen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Mean ± SD</td>
<td>61 ± 7.41007</td>
</tr>
<tr>
<td>Gender</td>
<td>Male</td>
<td>30</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>26</td>
</tr>
<tr>
<td>Eye</td>
<td>Right eye</td>
<td>24</td>
</tr>
<tr>
<td></td>
<td>Left eye</td>
<td>32</td>
</tr>
</tbody>
</table>

Table 1. Demographic details of the patients.
Table 2 shows pupil diameter. The average horizontal pupil diameter at the beginning of surgery is almost the same in both groups (Nepafenac-7.89 ± 0.94 mm and Flurbiprofen-7.91 ± 0.74 mm). The average vertical diameter at the beginning of surgery in the Nepafenac group was 8.11 ± 1.05 mm and in the Flurbiprofen group was 7.77 ± 0.80 mm. There is no statistically significant difference in horizontal (p-value=0.926) and vertical diameter (p-value=0.085) at the beginning of surgery in both groups. There is no statistically significant difference in horizontal and vertical pupil diameter at the end of surgery in both groups (horizontal p-value=0.946 and vertical p-value=0.912).

Table 3 shows baseline change in horizontal and vertical pupil diameters from beginning to end of the surgery with percentage loss of mydriasis in both groups. There was no significant difference in baseline change in horizontal diameter (p-value=0.404) and vertical diameter (p-value=0.485) in both groups. At the end of surgery, there was no significant percentage loss of horizontal (p-value=0.485) and vertical (p-value=0.311) pupil diameter in both groups.

Table 4 shows the difference of mean horizontal and vertical (H+V) pupil diameters at the beginning and end of surgery in Nepafenac and Flurbiprofen groups in correlation with duration of surgery. Duration of surgery was divided into 3 time intervals, less than 30 mins, 30-60 mins and more than 60 mins. There was no statistically significant difference in the mean value as the duration of surgery is increased in both groups.

Table 5 shows pupil diameter at different stages of surgery (mean, SD) in both groups.

Table 6 shows baseline change and percentage loss of pupil diameter in both groups.

Table 7 shows the difference of mean horizontal and vertical (H+V) pupil diameters at the beginning and end of surgery in Nepafenac and Flurbiprofen groups in correlation with duration of surgery.

Discussion

Mydriasis is the key point for a successful cataract surgery. Pupillary constriction during surgery causes various difficulties like difficulty in nucleus prolapse and makes the eye at risk for further complications due to poor visualization [10]. This risk is increased especially when beginners are performing

surgery during their learning period. Topical NSAIDS are important in combating this situation and also to reduce postoperative pain and inflammation [10-13]. Many comparative studies were done between different NSAIDS and placebo regarding maintaining mydriasis during surgery (Table 5).

<table>
<thead>
<tr>
<th>Year</th>
<th>Authors</th>
<th>Drugs compared</th>
<th>Observed effect</th>
<th>Type of surgery</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>2019</td>
<td>Minj et al. [14]</td>
<td>Nepafenac, Bromfenac</td>
<td>Mydriasis, Postoperative inflammation</td>
<td>SICS, Phacoemulsification</td>
<td>Both are equal</td>
</tr>
<tr>
<td>2018</td>
<td>Prakash et al. [5]</td>
<td>Nepafenac, Flurbiprofen</td>
<td>Mydriasis</td>
<td>SICS</td>
<td>Both are equal</td>
</tr>
<tr>
<td>2017</td>
<td>Chen et al. [13]</td>
<td>Bromfenac, Control group</td>
<td>Mydriasis, Postoperative inflammation</td>
<td>FLACS</td>
<td>Bromfenac is effective</td>
</tr>
<tr>
<td>2016</td>
<td>Sharma et al. [10]</td>
<td>Dexamethasone, Ketorolac</td>
<td>Mydriasis, Postoperative pain and inflammation</td>
<td>SICS</td>
<td>Ketorolac is more efficacious</td>
</tr>
<tr>
<td>2015</td>
<td>Sarkar et al. [4]</td>
<td>Nepafenac, Flurbiprofen</td>
<td>Mydriasis</td>
<td>SICS</td>
<td>Both are equal</td>
</tr>
<tr>
<td>2015</td>
<td>Bansal et al. [11]</td>
<td>Nepafenac, Bromfenac</td>
<td>Mydriasis</td>
<td>-</td>
<td>Both are equal</td>
</tr>
<tr>
<td>2015</td>
<td>Jung [15]</td>
<td>Bromfenac, Ketorolac</td>
<td>Mydriasis, Postoperative inflammation</td>
<td>Phacoemulsification</td>
<td>Both are equal</td>
</tr>
<tr>
<td>2012</td>
<td>Zanetti et al. [12]</td>
<td>Prednisolone, Ketorolac, Nepafenac and placebo</td>
<td>Mydriasis</td>
<td>Phacoemulsification</td>
<td>Prednisolone, Ketorolac and nepafenac are equally efficacious and more than placebo</td>
</tr>
<tr>
<td>2011</td>
<td>Atanis et al. [16]</td>
<td>Ketorolac, Nepafenac</td>
<td>Mydriasis</td>
<td>Phacoemulsification</td>
<td>Nepafenac is more efficacious</td>
</tr>
<tr>
<td>2011</td>
<td>Abdel et al. [17]</td>
<td>Flurbiprofen, Dexamethasone</td>
<td>Mydriasis</td>
<td>-</td>
<td>Both are equal but Flurbiprofen has</td>
</tr>
</tbody>
</table>

Table 5. Comparison of different drugs in various studies.

The results of present study show that nepafenac and flurbiprofen are equally efficacious which corresponds with the other studies in maintaining mydriasis during cataract surgery. The additional information that we obtain from this study is drug efficacy in correlation with duration of surgery which no study has done till now.

Conclusion

In this study, both drugs were equally effective at different time intervals but as the duration of surgery was prolonged, nepafenac had a significant effect in maintaining mydriasis. The prime importance of the study is to observe the effect of the drugs in cataract surgeries with long duration where trainees are the surgeons. As the trainees need sufficient time for the completion of the surgery in their learning phase, the use of NSAIDS preoperatively plays a major role in success of the surgery without any complications. The major limitation of the study is less number of subjects, future research is needed with a large number of study subjects.

References

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