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IMPACT OF NEPAFENAC (0.1%) WITH TOPICAL STEROIDS VERSUS TOPICAL STEROIDS ALONE ON CENTRAL MACULAR THICKNESS AND VOLUME CHANGES POST-CATARACT SURGERY: A RANDOMISED CONTROLLED STUDY

Ophthalomology

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ABSTRACT

Introduction This study aimed to evaluate the efficacy of adding 0.1% nepafenac ophthalmic suspension to a topical steroid regimen after uncomplicated cataract surgery in reducing additional inflammatory manifestations and subclinical macular edema. **Methodology** This randomized controlled interventional study took place at an upgraded Department of Ophthalmology within a tertiary care facility in Jaipur. Data collection occurred from June to October 2023, with an additional two months for analysis. The study included patients with senile cataracts of NS2/3 grade who provided informed consent, with exclusion criteria covering various ocular and systemic conditions. A total of 82 participants were randomly assigned to two groups, with 41 individuals in each, using sealed envelope randomization. Arm A received topical Nepafenac 0.1% and Dexamethasone 0.1%, while Arm B received Dexamethasone 0.1% alone. **Results** The mean age of participants was 65.08±6.37 years. Both groups showed comparable baseline characteristics and improvements in best-corrected visual acuity (BCVA) postoperatively, with statistically insignificant differences between the groups. Although central retinal thickness (CRT) increased postoperatively in both groups, only the group receiving Dexamethasone alone showed a significant increase at 6 weeks, but the difference between both groups in terms of CRT and macular volume was statistically insignificant ($p>0.05$) **Conclusion** Our study found minimal postoperative macular thickness increases in both control and treatment groups, with no notable differences detected in OCT measurements. The slight increase in macular thickness did not affect final BCVA, resulting in excellent outcomes for both groups. We found no indication that topical NSAIDs pose a greater risk of adverse effects compared to corticosteroids.

KEYWORDS

INTRODUCTION

A cataract is a clouding or opacification of the eye's normally clear lens or its capsule, which is a translucent membrane that surrounds the lens and prevents light from passing through it to the retina.[1] Around the world, cataracts are a leading cause of blindness.[2] Only in the early stages of treatment are refractive glasses a viable alternative. If the cataract has progressed to the point where it is causing problems with daily activities, surgery is a highly effective option.[3]

Ocular surgery initiates an inflammatory cascade that includes the generation of prostaglandins and other inflammatory mediators mediated by cyclooxygenase (COX). One effect of the inflammatory environment is the breakdown of the blood-retinal barrier, which can lead to frank edema, macular thickening, or intraretinal fluid buildup.[4,5] This inflammatory cascade set off by phacoemulsification results in pain, discomfort, and cystoid macular edema (CME). A smooth phacoemulsification has a 0%–2% incidence of clinical CME.[6,7] CME usually appears between the fourth and tenth postoperative week and can cause photophobia, image distortion, visual blurring, or any combination of these symptoms.[8] Macular edema may arise for a variety of causes, such as the patient's characteristics, the surgical method employed, the posterior capsule's integrity, the intraoperative medications used, and the implantation of the intraocular lens.[9] OCT, being a safe, non-invasive, and rapid technology, is instrumental in objectively documenting foveal and retinal morphology, facilitating early detection and monitoring of macular changes in CME.[10]

Topical NSAIDs by suppressing PG production can help ensure a quick and thorough recovery of visual acuity both before and after surgery. NSAIDS have advantages such as stable IOP, lower risk of infection, and the additional benefit of analgesia. A topical nonsteroidal anti-inflammatory prodrug called napafenac ophthalmic suspension 0.1% has been licensed to reduce pain and inflammation that may arise from cataract surgery. Ocular tissue hydrolases allow it to pass through the cornea and transform it into amfenac in aqueous humour, a more active metabolite. The cyclooxygenase enzyme, which is necessary for the synthesis of PG, is inhibited by amfenac.[11] As a result, it works well to prevent and cure CME by inhibiting the inflammatory cascade.

This study aimed to assess the potential efficacy of incorporating 0.1% nepafenac ophthalmic suspension into a topical steroid regimen for mitigating additional inflammatory manifestations and subclinical macular edema subsequent to an uncomplicated cataract surgery. This study was planned with the following objectives-

a. To compare change in central macular thickness at 3 and 6 weeks after procedure among patients undergoing uneventful cataract surgery administered with Nepafenac 0.1% plus Topical Steroid versus Topical Steroid
b. To compare change in total macular volume at 3 and 6 weeks after procedure between both study groups.

MATERIALS AND METHODS

This hospital based randomized controlled interventional study was carried out in upgraded Department of Ophthalmology, tertiary care facility, Jaipur. Data collection for the study was started in June 2023 after clearance from the Institutional Ethical Committee of the institution, and data collection was completed in October 2023. Additional two months was taken for data analysis. All patients with senile cataract, undergoing cataract surgery during the study period in the facility were our study population.

Patients with a cataract grade of NS2/3, who provided written informed consent, were eligible for inclusion in our research. Exclusion criteria encompassed individuals with chronic ocular inflammation, other ocular pathologies, a history of topical NSAIDs or steroids, oral or inhalational steroid or NSAID use, prior ocular trauma or surgery, retinopathy, macular degeneration, intra or postoperative complications, known hypersensitivity to administered drugs, any vision-impairing eye disorder apart from cataract, and individuals with multiple conditions.

Sample Size:

Sample of 37 patients in each group was calculated at 95% confidence and 80% power to verify the mean difference of 11±17.1µm between both the study groups. Considering 10% drop out rate sample size was further enhanced to 41 patients in each group.[12]

(Figure I) A total 82 participants were prospectively enrolled and randomly assigned to two groups, each consisting of 41 individuals. To ensure impartial group allocation, the sealed envelope randomization method was employed. Opaque envelopes, securely sealed and labelled with unique identifiers or numbers, were prepared, maintaining uniformity in appearance to uphold allocation concealment. Participants received these identifiers upon enrolment. Randomization was executed by sequentially drawing envelopes, with each envelope disclosing the assigned group. In Arm A (intervention arm), participants were administered topical eye drops containing Nepafenac 0.1% and Topical Dexamethasone 0.1%, while Arm B received Topical Dexamethasone 0.1% alone.

Procedure and Methodology

Each patient had a pre-treatment evaluation that included a thorough relevant ocular and medical history, a complete blood cell count, blood sugar levels, and baseline evaluation of best corrected visual acuity, slit lamp examination, direct and indirect ophthalmoscopy, and 3D OCT Macula. Each patient was followed up at one, three, and six weeks after cataract surgery.

Statistical analysis

The investigator collected and entered the data into a Microsoft Excel Sheet on the same day to minimize potential bias associated with data entry. Categorical data were presented as proportions, and the differences in proportions between study arms was analysed using the Chi-square test. Continuous data were summarized using mean and standard deviation, with differences in means assessed through the student t-test. The significance level was set at a 95% confidence interval.

RESULTS

In our study, total 82 participants with senile cataract were recruited, who underwent cataract corrective surgery. These participants were randomised in two groups using covariate adaptive randomization technique. In study arm, 41 patients were administered with topical eye drops containing Nepafenac 0.1% and Topical Dexamethasone 0.1%, while Arm B received Topical Dexamethasone 0.1% alone. All the patients were followed up post-operatively at 1, 3 and 6 weeks, and no adverse events was reported by any of patients in both groups. The mean age of participants in our study was 65.08±6.37 years. More than half (57.3%, 47/82) of patients were male and rest were female. Male to female ratio was 1.3:1.

(Table I) Both study arms were comparable at baseline in terms of age, sex, and residence ($p>0.05$). The mean age of participants in study arm was 64.44±7.37 and of control arm was 65.73±5.21 years. Proportion of male in study arm was 61% and in control arm it was 53.7%, and rest of participants in both study arms were female.

(Table II) it depicts the mean value of CRT and Macular volume in 1 mm area as well as 3 mm preoperatively and post-operatively at different time intervals. Mean value of BCVA, CRT, and MV in 1 mm area as well as 3 mm at baseline of both arms were comparable to each other ($p>0.5$). The BCVA improved significantly in both study arms from baseline to post-operatively; in study arm from Pre-operative 0.48±0.18 logMAR to 0.18±0.10, 0.06±0.04, and 0.04±0.04 at 1, 3 and 6 weeks after procedure ($p<0.05$), similarly significant improvement in BCVA were noted among participants of control arm. While difference in BCVA logMAR between both study arm post-operatively at different time intervals was found to be statistically insignificant ($p>0.05$). At baseline mean CRT was comparable among participants of both study arms ($p>0.05$). The mean CRT value increased post-operatively at different time points from baseline among patients of both arms. The mean value of CRT at 1, 3, and 6 weeks after the procedure were also similar in both study arms, and the difference in mean value of CRT among both study arms was statistically insignificant ($p>0.05$). In study arm, increases in CRT from baseline to 6 weeks was found to be insignificant ($p>0.05$) while in study arm B increase in mean CRT at 6 weeks post-operatively from baseline value was statistically significant ($p<0.05$). For macular volume in central 1mm area, increase at 6 weeks from baseline was significant in study arm ($p<0.05$), while increase in macular volume in control arm was statistically insignificant ($p>0.05$). The difference in mean macular volume in 1 mm area at different time points between both study arm was found to be statistically insignificant ($p>0.05$). Similarly, there was an increase in mean value of macular volume in 3 mm area postoperatively from baseline in patients of both study groups. And the difference in macular volume in 3 mm area among patients of both study group was statistically insignificant ($p>0.05$). No adverse events was seen in both study arms related to administration of drugs.

DISCUSSION

This hospital based randomized controlled interventional study was carried out to assess the potential efficacy of incorporating 0.1% nepafenac ophthalmic suspension into a topical steroid regimen for mitigating additional inflammatory manifestations and subclinical macular edema subsequent to an uncomplicated cataract surgery. Complications of cataract surgery, particularly CME, can have a significant impact on visual acuity. Despite advances in surgical techniques aimed at reducing complication rates and improving visual outcomes, CME remains the most common cause of vision loss following uncomplicated phacoemulsification cataract surgery.[13,14] In the context of CME prophylaxis and treatment, reducing the elevated levels of inflammatory mediators has been the primary approach. Numerous studies have explored the potential benefits of employing topical NSAIDs, either alone or in conjunction with corticosteroids, for the management of CME.[15,16] The impact of OCT on the diagnosis and management of retina-related diseases cannot be overstated. A substantial amount of clinical research has been devoted to investigating OCT measurements of macular thickness, with a particular emphasis on cystoid macular edema (CME) following cataract surgery. This has resulted in a wealth of data that can be utilized to enhance patient care and treatment outcomes. The primary outcomes of our research indicate that following MICS, there were no discernible disparities between the treatment and control groups in terms of central retinal thickness, total macular volume, or best-corrected visual acuity (BCVA).

Several investigations have assessed the function of topical NSAIDs in the prevention of CME and have discovered no dissimilarity in postoperative macular volume between individuals (without risk factors) who employed NSAIDs and those who received a placebo.[17] This finding is in concordance with our result. In our study, increase in central retinal thickness following cataract correction surgery was seen in both the study arms, although the increase in thickness among patients receiving topical nepafenac in combination with steroid was lesser compared to patients receiving topical steroid alone, but this difference between both the arms was found to be statistically insignificant ($p>0.05$).

The increase in macular thickness following phacoemulsification as measured by OCT is a widely recognized phenomenon. Unlike many other nonsteroidal anti-inflammatory drugs (NSAIDs), nepafenac is not available in its free acid form. Instead, it passes through the cornea and is transformed into its active form, amfenac, by enzymes present within the eye. This distinct mechanism of action could potentially lead to better efficacy in the back of the eye compared to other NSAIDs that do not possess these characteristics. This property of nepafenac can be attributed to lesser rise in central retinal thickness.[18] Nevertheless, some of these studies have revealed the therapeutic benefits of topical NSAIDs over a placebo in lessening pseudophakic macular edema in patients with risk factors, such as diabetic retinopathy.[19]

A significant clinical concern following routine phacoemulsification is the impact of increased macular thickness on best-corrected visual acuity (BCVA). Our research conveys a notable enhancement in best-corrected visual acuity (BCVA) levels in both the study groups during the postoperative follow-ups, without any significant variations in visual acuity between the two study arms. This finding suggests that the increase in macular thickness, as assessed by optical coherence tomography (OCT), does not possess a clinically substantial influence on visual acuity. Almeida et al reported that there was no substantial improvement in visual acuity one month after surgery in patients who were administered prophylactic nepafenac, in comparison to those who received a placebo.[20] This also supports our findings.

Our research has several limitations. One of them is the limited duration of our follow-up period, which prevented us from assessing the long-term effects of CME. Additionally, our sample size was smaller, which affects the generalizability of our results. Furthermore, we did not include high-risk populations or patients with retinopathy in our study, which may limit the applicability of our findings to high risk and diabetic populations. Further study with larger sample size, and long term follow up is needed to provide better generalizability of the results.

CONCLUSION

Our study's outcomes revealed that the rise in postoperative macular thickness was minimal for both the control and treatment groups. The OCT measurement demonstrated no notable differences in macular thickness among the patient groups. Additionally, the slight increase in macular thickness had no bearing on the final best-corrected visual acuity (BCVA) in either group. As a result, both groups attained excellent BCVA outcomes. Our findings do not suggest that the employment of topical nonsteroidal anti-inflammatory drugs (NSAIDs) poses a more significant risk of adverse consequences in contrast to topical corticosteroids.

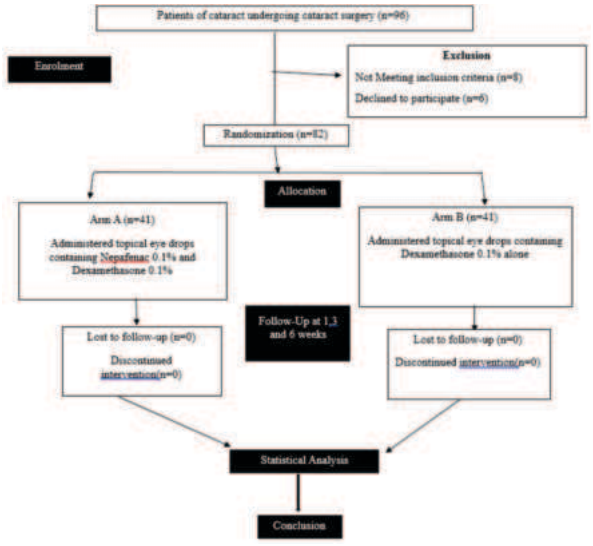

Figure I- CONSORT flow diagram

Table I- Baseline characteristics of participants

Variable	Study Arm (n=41)	Control Arm (n=41)	p value
Age	64.44±7.37	65.73±5.21	0.363
Sex			
Male	25(61)	22(53.7)	0.655
Female	16(39)	19(46.3)	
Residence			
Urban	29(70.7)	31(75.6)	0.803
Rural	12(29.3)	10(24.4)	

Table II- Central Retinal Thickness (CRT) and Macular volume in both groups

Variable	Study Arm (n=41)	Control Arm (n=41)	p value
BCVA			
Pre-operative	0.48±0.18	0.55±0.22	0.119
Post operative			
1st week	0.18±0.07	0.15±0.08	0.414
3rd week	0.11±0.04	0.12±0.05	0.368
6th week	0.09±0.02	0.10±0.03	0.080
CRT (µm)			
Pre-operative	225.84±12.74	224.72±13.72	0.703
Post operative			
1st week	226.62±11.54	227.42±10.84	0.785
3rd week	227.94±12.42	228.42±14.68	0.873
6th week	229.32±20.48	233.46±18.32	0.338
MV, 1-mm area (mm3)			
Pre-operative	0.20±0.07	0.19±0.07	0.520
Post operative			
1st week	0.21±0.09	0.21±0.10	1.00
3rd week	0.22±0.08	0.23±0.09	0.596
6th week	0.23±0.07	0.24±0.10	0.601
MV, 3-mm area (mm3)			
Pre-operative	2.08±0.14	2.05±0.15	0.352
Post operative			
1st week	2.12±0.16	2.09±0.13	0.354
3rd week	2.14±0.19	2.12±0.17	0.617
6th week	2.18±0.18	2.15±0.18	0.453

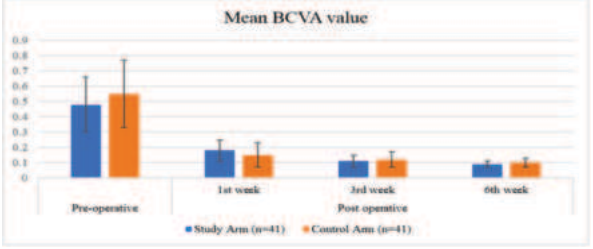

Figure II- Error bar chart of mean BCVA value at different time intervals

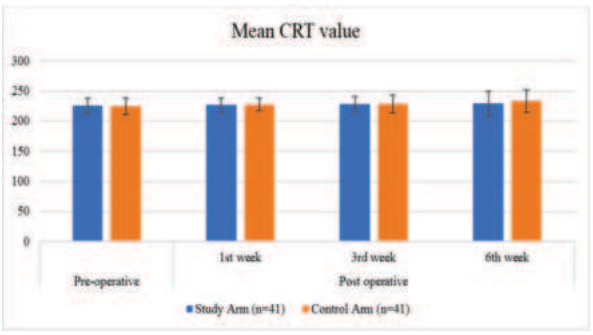

Figure III- Error bar chart of mean CRT value at different time intervals

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