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Original Research Paper

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# RANDOMISED STUDY OF MACULAR EDEMA AFTER CATARACT SURGERY IN PATIENTS TREATED WITH AND WITHOUT TOPICAL NON STEROIDAL ANTI INFLAMMATORY DRUG 0.1% NEPAFENAC

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**ABSTRACT** CME is a serious consequence of cataract surgery. Corticosteroids can effectively prevent and treat CME, but are associated with serious side effects thus safer alternative treatments are desirable. Nepafenac is the only topical NSAID with a prodrug structure thus providing effective targeting of macula, providing an advantage over conventional NSAIDs.

**KEYWORDS :**

## INTRODUCTION

Cataract is the opacification of the lens fibres or its capsule. It is one of the most common causes of visual impairment in the world. According to the World Health Organisation (WHO), cataract is the leading cause of blindness all over the world, responsible for 47.8% of blindness and accounting for 17.7 million blind people( 1,2). Pseudophakic macular edema is one of the important complications. The incidence of pseudophakic macular edema is not well documented in literature . Macular edema appears as retinal thickening with the presence of intraretinal cavities on OCT .The regular fundus examination can be challenging for diagnosing the presence of CME . The non invasive technique of OCT confers advantage over the fluorescein angiography imaging which is an invasive procedure .

## MATERIAL AND METHODS

A prospective, interventional, Randomised, comparative study that was done on 500 eyes following cataract surgery in tertiary health care from October 2018 till May 2020 out of which 250 eyes(study group) were treated with a combination therapy of topical NEPAFENAC 0.1% ( 3 months) with topical DEXAMETHASONE 0.1% (6 weeks ) and 250 eyes(control group) were treated with only 0.1% dexamethasone for 6 weeks as per the standard postoperative protocol . Nepafenac in the study group was given twice daily for 3 months. CME was documented by observing retinal edema on optical coherence tomography (OCT) using Spectral Domain HD OCT. OCT was done on pre op day, 7th post op day, 1 month and 3 months. A thorough workup of the patient was carried out. Two groups were made : A)case group - 0.1%nepafenac +0.1%dexamethasone B)control group - 0.1%dexamethasone

### Selection Of Cases

### Inclusion Criteria

Subjects were considered to be eligible if the following criteria were met:

A) Ability to provide written informed consent and comply with study assessments for the full duration of the study
B) Age > 50years having no history of diabetes ,hypertension or undergone any ocular surgery within last 6 months
C) Spectral domain OCT central retinal thickness < 300 microns
D) no evidence of CME prior to surgery or where the cataract had precluded visualization of the fundus preoperatively
E) no other ocular disorder predisposing to cystoid macular edema.

### Exclusion Criteria

Subjects who meet any of the following criteria were excluded from this study:

A) Subjects who were unable to provide informed consent and come for follow up for 3 months
B) Eventful cataract surgery
C) Age below 50 years
D) Subject having significant diabetic retinopathy (greater than moderate NPDR) or macular edema associated with diabetic retinopathy
E) Any other additional ocular diseases which could irreversibly compromise the visual acuity of the study eye including anterior ischemic optic neuropathy (AION), age related macular degeneration (AMD), retinal detachment, etc
F) History of glaucoma surgery
G) Concurrent use of systemic anti-VEGF agents
H) Preoperative risk factors for pseudophakic cystoid macular edema(PCME) example macular hole ERM, contralateral PCME
I) Prostaglandin use

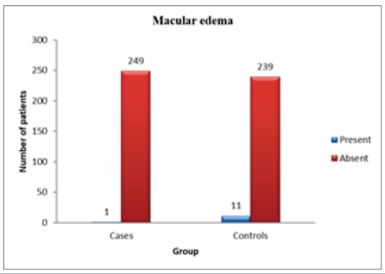
### Randomization Procedure

For Randomization, Permuted block randomization was used. With randomly permuted blocks, subjects were assigned to treatment in blocks to insure that equal numbers of subjects are assigned to each treatment each time the number of subjects is a multiple of the block size. In order to do this we specify a sample size that is divisible by the block size we choose. In turn we choose a block size that is divisible by the number of treatment groups you specify.

Random allocation in blocks: Sample size (Subjects): 500
Block size: 4 Treatments/ Intervention: 2 (Intervention A &B)
Group A :- receiving NSAIDS & Steroid: (N+S) CASES
Group B :- (control) receiving: steroids (C) CONTROLS

On every follow up visit after cataract surgery , the detailed ophthalmic evaluation was done including : Post operative vision on LOGMAR visual acuity chart ,Slit lamp examination for Anterior segment examination, Wound evaluation, Fundus examination and Optical coherence tomography by Macular cube ( 512*128) CSMT.

### Occurrence Of Macular Edema



In the cases group only 1 patient had macular edema whereas in the control group 11 were diagnosed with macular edema. Rest 488 out of the total 500 population had no macular edema.

The p vale was 0.003 which implies that the results were statistically significant.

In the 1 case who developed macular edema, it was detected on the 4th follow up that is 3 months after the cataract surgery. Amongst the controls 6 of them were detected on the 1st follow up of 7 days, 4 on the 2nd follow up of 15 days and the rest 1 was detected on 3rd follow up of 1 month.

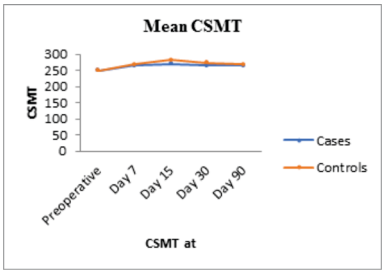



Diagram for the mean CSMT of cases and controls . The mean CSMT amongst controls was higher than cases at day 7 , day 15 , day 30 and day 90. The difference being more at the 2nf follow of 15 days .

## DISCUSSION

Irvine-Gass is an inflammatory process occurring in up to 20% of cataract extraction with intraocular lens. 1% of these have a clinically significant decrease in visual acuity; in more complicated surgeries, such as those in which there is violation of the posterior capsule, this figure can reach 20%. CME usually occurs up to 6-10 weeks postoperatively.(3,4)

34.8%of the cases belonged to group 1, 35.2 %of the cases belonged to group 2 and 30% of the cases belonged to group 3. for the controls , 34.4 % belonged to group 1, 30% to group 2and rest 35.6 % of the controls belonged to group 3 . The p value for the age distribution was not statistically significant in this study . In a study of risk factors and incidence of macular edema after cataract extraction by Colin .J et all stated that the Eyes in which PME developed were more likely to be male, older, and to demonstrate risk factors.(5)

In our study we have included the age group of more than 50 years . Therefore our study included population of older age group which is the reason for statistical insignificance of the results among these groups . 60.8% of the cases were males whereas 39.2 % of the cases were females . Amongst the control groups 65.6 % were males and 34.4 % were females . in our study there was no gender wise predilection in the occurrence of pseudophakic macular edema .. Similarly the post operative vision of the cases and controls were not statistically significant . The known risk factors for the occurrence of pseudophakic macular edema mentioned in previous study like presence of diabetes mellitus , use of prostaglandin analogues , occurrence of complications like posterior capsular rupture and vitreous loss during surgery , were already excluded from our study . Thus ,our study includes the occurrence of pseudophakic macular edema in uneventful surgery and without any known risk factors. Therefore , these results reflect purely surgery related pathogenesis of macular edema .

The occurrence of macular edema in the cases was just 0.4 % in our study as compared to the 4.4 % in the controls . rest of the 99.6% of cases and 95.6% of controls were observed to have no macular edema even after the last follow up of 3 months.. The p value of this distribution was 0.003%which was statistically significant. Thus the combination therapy of 0.1%nepafenac and 0.1% dexamethasone proved to have a significant impact on the occurrence of macular edema in our study.12 patients developed macular edema following uneventful cataract surgery out of which just 1 patient belonged to case group and the rest 11 were in the control group. The follow up in our study was on 7 th day, 15th day, 1 month and 3 months postoperatively .We observed the time of detection of macular edema according to our follow up schedule . In the 1 case that developed macular edema , it was 64 detected on the 4 th followup in the control group 2.4 % were detected on 2 nd follow , 1.6 % on 3 rd follow up and 0.4 % on the 4 th follow up . In a similar study by Eric j . wolf et al , described Visually significant pseudophakic macular edema documented by OCT in 5 patients treated with prednisolone alone and in no patients treated with steroid and nepafenac . (6)

In a retrospective study by Seenu M . Hariprasad et al , NSAIDs apparently provide additional benefit to that produced by corticosteroids and anti-VEGF, only nepafenac- and bromfenac-treated eyes showed reduced retinal thickness at 12 and 16 weeks, and only nepafenac showed a significant improvement in visual acuity. In another retrospective study, nepafenac 0.1% resulted in improved retinal thickness along with visual acuity in patients with chronic CME(7) In our randomized study the incidence of macular edema was found to be 4.4 % in the control group compared to only 0.4 % in the case group indicating a significant synergistic action of nonsteroidal anti inflammatory drugs with corticosteroids. The mean CSMT amongst controls was higher than cases at day 7 , day 15 , day 30 and day 90. The difference being more at the 2nd follow up (15 days ). Thus this study concluded that there was significant reduction in occurrence of macular edema in patients treated with 0.1%nepafenac along with 0.1% dexamethasone as compared to only 0.1% dexamethasone .

Adding nepafenac has proved to be helpful in reducing the occurrence of macular edema post cataract surgery . The combination of nepafenac and dexamethasone seems to have a synergistic effect in the prevention of occurrence of macular edema .

## CONCLUSION AND SUMMARY

The occurrence of macular edema following uneventful surgery was 0.4%in the cases (group 1 ) and was 4.4 % in controls (group 2 ) .P value for occurrence of macular edema in cases and control was statistically significant 0.003% .The combination therapy of 0.1% nepafenac and 0.1% dexamethasone given in cases group proved to have a significant impact on occurrence of macular edema . The macular edema was detected in controls more commonly on the second follow up of 15 days. However , in our study the age and gender wise distribution was not statistically significant .

This study reflects purely the surgery related pathogenesis of macular edema as the occurrence of eventful surgery and presence of other risk factors has already been excluded. Thus, the combination of 0.1% topical nepafenac and 0.1% topical dexamethasone has a synergistic effect in the prevention of macular edema.

Declaration : Funding None
Declaration none

**Ethical Considerations and Issues:** Study was conducted in accordance with ICH - GCP, CDSCO-GCP guidelines. Declaration of Helsinki (October 2000) and amended schedule-Y (2005). Study approved from the IEC / IRB (Institutional Ethical /Review Board) before commencing. Investigator obtained the approvals before conducting the study. Informed consent document (printed) included in the patient information sheet regarding the study and one signature

### Statistical Analysis

Results of demographic, clinical and biochemical characteristics were expressed as range, mean and standard deviation. For analysis of data chi-square test and unpaired t test was used.

### Statistical Software

The analysis of data was done using Statistical software SPSS 23. Microsoft word and Microsoft Excel version 13 were used to generate graphs and tables.

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