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- **Nepafenac for Prevention of CME After Phacoemulsification**
- **Retinopathy of Prematurity Prevalence**
- **Intermittent Distance Exotropia in Children**
- **Ocular Trauma in Pakistan: Trends and Medicolegal Aspects**
- **Cefuroxime Stromal Hydration After Phacoemulsification**

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Comparison of 0.3% Nepafenac and 0.1% Nepafenac in Prevention of Cystoid Macular Edema After Uneventful Phacoemulsification

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Abstract:

Objectives: To compare changes in mean central macular thickness (CMT) in patients receiving 0.3% nepafenac once nightly versus 0.1% nepafenac three times daily following uneventful phacoemulsification.

Methodology: A randomized controlled trial was executed at the Ophthalmology Department of POF Hospital over six months from April 2025 to September 2025. A total of 130 patients, aged 50–80 years, were recruited using non-probability consecutive sampling and randomly allocated to either the 0.1% nepafenac or 0.3% nepafenac group (65 patients each). Pre-operative CMT was assessed using optical coherence tomography (OCT). One group received 0.1% nepafenac three times daily, while the other received 0.3% nepafenac once nightly. Treatment began one day before surgery and continued for six weeks after uneventful phacoemulsification. Post-operative CMT was assessed by OCT at six weeks. Data were analyzed using SPSS version 25. Categorical variables were expressed as frequencies and percentages, continuous variables as mean $\pm$ standard deviation. Paired and independent sample t-tests were used, with $p < 0.05$ considered statistically significant.

Results: The mean age of participants was 69.61 years; 51.5% were male and 48.5% were female. Both regimens significantly reduced CMT at six weeks (mean pre-operative CMT: 235.69 μm ; mean post-operative CMT: 231.17 μm ; $p < 0.001$). However, there was no significant difference in post-operative CMT between the 0.1% nepafenac group (232.48 μm) and the 0.3% nepafenac group (229.86 μm ; $p = 0.848$).

Conclusion: Both 0.1% and 0.3% nepafenac were equally effective in reducing CMT and preventing cystoid macular edema following uneventful phacoemulsification. *Al-Shifa Journal of Ophthalmology* 2026; 22(2): 70-75.

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Introduction:

Phacoemulsification is a preferred procedure for cataract extraction and is globally associated with excellent visual outcomes. However, cystoid macular edema (CME) remains a significant post-operative complication that adversely affects vision^{1,2}. Cystoid macular edema (CME), with an average occurrence of 0.2 % to 4.1 %, is one of the leading causes of reduction of visual acuity (VA) following uneventful phacoemulsification. It is defined by the fluid accumulation in the macula, leading to increase in macular thickness and impairment of central vision³. During phacoemulsification, surgical trauma can induce inflammation, disrupting the blood-retinal barrier. This disruption allows inflammatory mediators such as

prostaglandins to permeate the macular region, increasing vascular permeability and causing fluid leakage⁴. Pathophysiologically, the blood-retinal barrier breakdown is central to CME formation. Inflammatory mediators, particularly prostaglandins and cytokines, play a crucial role by enhancing vascular permeability. The resultant fluid accumulation in the macula leads to the characteristic cystoid spaces seen on optical coherence tomography (OCT)⁵. Risk factors for developing CME include diabetic retinopathy, uveitis, vitreomacular traction, and complicated surgeries with rupture of posterior capsule and loss of vitreous⁶. Nepafenac, a non-steroidal anti-inflammatory drug (NSAID), has been employed to prevent and treat CME due to its potent anti-inflammatory properties. Nepafenac is a pro drug that converts to its active form, amfenac, within ocular tissues, providing targeted inhibition of the cyclooxygenase enzyme and reducing prostaglandin synthesis. This action mitigates the inflammatory response associated with phacoemulsification and helps maintain the integrity of the blood-retinal barrier⁷. The 0.1% concentration has demonstrated effectiveness in reducing inflammation and CME incidence. However, the higher concentration of 0.3% nepafenac is hypothesized to offer enhanced anti-inflammatory effects, potentially providing superior protection against CME⁸.

Nanda et al., 2022 reported that at the 6-week evaluation, the Nepafenac 0.3% drops once a day group had 1 patient (1.0%) with clinical CME, ($p=0.477$)⁹. Miyake et al., 2011 concluded that occurrence of edema was significantly lower in the nepafenac 0.1% group (14.3%)¹⁰. Sarfraz et al., 2017 reported that CME was observed in one patient (3.3%) among patients who were treated with and received 0.1% Nepafenac with three times daily dose¹¹. D Singhal et al., 2022 reported that efficacy of both 0.1% and 0.3% nepafenac was more than prednisolone at 6 weeks post-operative but

was still significant¹². Bardoloi N et al., 2022 in his study comparing the two concentrations reported that 0.3% nepafenac showed more efficacy in prevention of Central Macular Thickness (CMT) in patients¹³. B Khan et al., 2025 in his trial compared the efficacy of using a combination of 0.3% nepafenac at night and 0.1% nepafenac at day versus 0.1% nepafenac. He demonstrated that combination of concentrations was significantly more effective in reducing post treatment macular thickness¹⁴.

The rationale for this study is to assess and compare the effectiveness of 0.3% nepafenac administered once a day versus 0.1% nepafenac administered thrice a day in preventing cystoid macular edema (CME) following uneventful phacoemulsification. While separate studies on the effectiveness of 0.3% nepafenac and 0.1% nepafenac exist in Pakistan, not many researchers have directly compared these two regimens in a single study. This study seeks to bridge a gap in literature, potentially offering new insights into the optimal dosing strategy for preventing CME, thereby improving patient outcomes and post-operative care in phacoemulsification surgery.

Methodology:

A Randomized control trial was conducted at the Department of Ophthalmology of POF Hospital, Wah Cantt for 6 months (from April 2025 to September 2025). Patients were chosen via non-probability consecutive sampling where all available subjects presenting in Eye OPD who met the specific inclusion and exclusion criteria within a designated time frame were selected for the study, until a predetermined sample size was reached. Sample size was determined with the help of WHO sample size calculator with significance level of 5% and power of study was set at 80%. Total sample size was 130 with 65 patients in each group. A double-blind design was used in which neither the patient nor the surgeons were aware of the drug strength

given to the patient. Institutional Review Board permission was obtained before this trial was conducted. All participating patients signed a written consent form before the study was conducted.

Individuals with prior history of vitreoretinal surgery were excluded and patients with ophthalmic conditions like corneal opacity, uveitis, glaucoma, poor mydriasis, lens dislocation, retinal and macular diseases were not included. Surgeries during which complications occurred during phacoemulsification such as damage to iris, posterior capsular rupture, nucleus drop and vitreous loss were excluded from the data. Moreover, Patients who were given steroids (topical or systemic) 15 days prior to the procedure, were given steroid injections through any method of administration 3 months prior, and individuals reporting any form of NSAIDs use within 7 days were also excluded from participation.

All patients with cataract (diabetic and non-diabetic, between 50 to 80 years of age) who agreed to take part in this study and fulfilled the inclusion criteria were selected. A senior ophthalmologist performed the anterior segment as well as dilated fundus examination on a slit lamp bio microscope, along with measurements of intraocular pressure. Spectral domain OCT was performed on selected patients, and pre-operative CMT was noted. Patients were categorized; Group A was given 0.1% Nepafenac (to be used thrice a day) and 0.3% Nepafenac (to be used once daily at night) was given to Group B. The drug was given one day prior to the surgery and continued for 6 weeks post-operatively. Phacoemulsification was performed by two senior surgeons with at least ten years of experience. Post-operative treatment of

topical steroids and antibiotics were given along with trial medicine. Patients were followed regularly. After 6 weeks post-operatively, OCT was performed again, and post-operative CMT was noted. Statistical Package for Social Sciences (SPSS) version 25 was used to perform analysis. Qualitative data like age, gender, presence of diabetes, eye involvement was measured in terms of frequency and percentages. Quantitative data like pre-operative and post-operative CMT was presented as standard deviation and mean. Paired sample t-test was used to compare the two means i.e. central macular thickness before and after the procedure and comparison of the post-operative CMT between the two groups was done via Independent sample t-test with statistical significance set at $p < 0.05$.

Results:

A total of 130 patients were chosen for this study, these patients were divided into two groups, each group was given either 0.1% nepafenac or 0.3% nepafenac. All patients underwent unilateral phacoemulsification. The mean age of patients was 69.61 years. There were a total of 67 (51.5%) male and 63 (48.5%) female patients. 63 (48.5%) were right eyes and 67 (51.5%) were left eyes. Total 70 (53.8%) patients were non-diabetic and 60 (46.2%) patients were diabetic.

There was a significant decline in post-operative central macular thickness (232.48 μm) in group A after phacoemulsification from baseline measurements (pre-operative CMT 236.69 μm). Group B showed a similar trend as depicted in Table 1.

Table 1: Comparison between pre- and post-operative CMT.

Study Groups	Pre-operative CMT (μm)	Post-operative CMT (μm)
0.1% nepafenac	236.69	232.48
0.3% nepafenac	234.69	229.86

Individual t-test was used to evaluate the two post-operative CMT values (0.1% Nepafenac and 0.3% Nepafenac). However, the difference in post-operative macular thickness between the two groups

was not statistically significant; post-operative CMT of 0.1% nepafenac was 232.48 μ m and post-operative CMT of 0.3% nepafenac was 229.96 μ m. $P=0.848$, as depicted in Table 2.

Table 2: Comparison between mean post-operative CMT of both groups

Study groups	Post-operative mean CMT (μ m)	p-value
Group A	232.48	0.848
Group B	229.86	0.848

Discussion:

CME is thought to be associated with eye inflammation. It is usually correlated with inflammation of uveal tract, retinal vein occlusion and diabetic retinopathy and is commonly encountered as a complication of phacoemulsification. In the process of natural lens being emulsified with implantation of artificial intraocular lens in posterior chamber, macular edema that occurs after this procedure is known as pseudophakic CME and this is also called Irvine-Gass syndrome. This rise in macular thickness is one of the most common causes of decreased visual acuity after cataract surgery¹⁵. Even though the exact pathophysiology is not yet defined, however the role of surgical trauma along with blood-retinal barrier disruption and release of prostaglandins is suspected¹⁶. Light toxicity and vitreomacular traction might also have a role¹⁷. Topical NSAIDs have been used with good therapeutic effects in controlling post-operative inflammation after cataract surgery, thereby reducing macular thickness. NSAIDs inhibit cyclo-oxygenase (COX) enzymes thus preventing the conversion of arachidonic acid to thromboxanes, prostacyclins, and prostaglandins which leads to decreased inflammation⁹.

We compared the effectiveness of both strengths of NSAIDs. The main goal of this trial was to prevent the rise in central macular thickness after uneventful cataract surgery. A decreasing trend was seen in central macular thickness of both groups

(Mean pre-operative CMT of 235.69 μ m to mean post-operative CMT of 231.17 μ m) with $P=0.000$ depicting that both the concentrations of NSAID are effective in lowering the CMT after surgery. While comparing the two groups, it was noted that there was slight difference in post-operative CMT of the two groups, 0.1% nepafenac had mean post-operative CMT of 232.48 μ m while 0.3% nepafenac had mean post-operative CMT of 229.86 μ m, but this difference is not significant $p=0.848$.

According to AK Nanda *et al.*, 2022, 200 patients went through Phacoemulsification, at 6 weeks, 8 patients of 0.1% nepafenac and 3 patients of 0.3% nepafenac group had subclinical CMT but these were statistically insignificant⁹. D Singhal *et al.*, 2022 reported in their study of 500 patients who were separated into 5 groups receiving nepafenac 0.1%, nepafenac 0.3%, bromfenac, preservative-free ketorolac, prednisolone acetate. The percentage of individuals with clinically significant CME was least in the groups who were given nepafenac 0.3% (1%) and 0.1% (1%) and greatest in those who were given prednisolone (4.3%) at 6 weeks though this difference was statistically insignificant ($P=0.34$)¹².

Bardoloi N *et al.*, 2022 in their study stated that the difference between the mean CMT of the two concentrations demonstrated a significant difference (281.29 μ m in 0.1% nepafenac group vs. 266.05 μ m in 0.3% nepafenac group, $P < 0.001$) at 1 month and at 3 months (276.25 $\pm$ 12.25 μ m vs. 262.11

$\pm 6.34\mu\text{m}$ in 0.1% nepafenac and 0.3% nepafenac groups, respectively, $P < 0.001$)¹³. PF Tzelikis *et al.*, 2018 in his study concluded that prophylactically after surgery of cataracts, nepafenac 0.3% was more effective in reducing macular thickness compared to placebo 5 weeks post-operatively¹⁸.

The greater efficacy was with both nepafenac concentration was validated by the decrease in cases of treatment failures. Using nepafenac 0.3% once daily may offer greater post-operative convenience for patients and may help improve dosing adherence. Nepafenac 0.3% is easily endured as it is to be used just once daily as compared to three times daily dose of 0.1% Nepafenac. Both concentrations and doses are equally safe as compared to the results of previous clinical trials. Our study also validates that both of these concentrations of nepafenac are effective as these were given for 6 weeks in both groups with significant results.

Conclusion:

The study concluded that both the drug 0.3% Nepafenac once a day and 0.1% Nepafenac thrice a day for 6 weeks after phacoemulsification were equally effective in preventing cystoid macular edema after uneventful Phacoemulsification. Once daily dosing was convenient for patients as compared to thrice daily dosing.

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