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Research Protocol

Ophthalmology Section

Efficacy of 0.1% Topical Nepafenac in Maintaining Transoperative Mydriasis and Preventing Postoperative Macular Oedema in Phacoemulsification Cataract Surgery: A Research Protocol

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ABSTRACT

Introduction: Following standard cataract surgery, postoperative Cystoid Macular Oedema (CMO) may result in visual impairment. Currently, phacoemulsification is considered the best surgical technique for cataract extraction due to the superior visual outcomes achieved after Intraocular Lens (IOL) implantation. Despite advancements in surgical techniques and improvements in IOL materials over the past decade, there remains a risk of unintentional ocular injury during surgery.

Need of the study: Miosis during cataract surgery can hinder surgical access and visualisation, increasing the likelihood of complications. It is caused by the release of Prostaglandins (PGs) triggered by surgical trauma, which stimulates contraction of the iris sphincter muscle. Nepafenac, a Non Steroidal Anti-Inflammatory Drug (NSAID), inhibits Cyclooxygenase (COX), thereby reducing PG synthesis and preventing miosis when administered prophylactically before surgery. Maintaining adequate mydriasis ensures better surgical access and reduces intraoperative risks. Additionally, nepafenac's anti-inflammatory properties help reduce the incidence of macular oedema—a postoperative complication arising from inflammation and disruption of the blood-retinal barrier.

Aim: To evaluate the effectiveness of prophylactic topical nepafenac 0.1% in maintaining intraoperative mydriasis and preventing postoperative macular oedema in patients undergoing topical phacoemulsification cataract surgery.

Materials and Methods: A prospective, randomised, single-masked comparative study will be conducted from June 2024 to June 2026 in the Ophthalmology Outpatient Department at Acharya Vinobha Bhave Rural Hospital (AVBRH), Sawangi, Meghe, Maharashtra, India. A total of 38 patients undergoing phacoemulsification cataract surgery will be equally divided into two groups (n=19 each). All patients will receive two doses of tropicamide 0.8% and phenylephrine 5% at 15-minute intervals. The experimental group will additionally receive nepafenac 0.1%—four doses administered hourly before surgery and three times daily for six weeks postoperatively. The control group will receive only prednisolone and moxifloxacin eye drops in a 15-day tapering regimen. Postoperative assessments will include Best-Corrected Visual Acuity (BCVA), Intraocular Pressure (IOP), fundoscopy, slit lamp evaluation of cells and flare and macular Optical Coherence Tomography (OCT) at two and six weeks. Statistical analysis will include descriptive tests, Chi-square test and Fisher's-exact test to determine associations among clinical and demographic variables.

Keywords: Antibiotic therapy, Cataract extraction, Intraocular implantation, Macular degeneration, Preventive therapy, Topical corticosteroid

INTRODUCTION

Phacoemulsification is currently regarded as the most effective surgical technique for cataract extraction due to the superior visual outcomes achieved following IOL implantation [1]. Despite significant advancements in surgical techniques and improvements in IOL materials over the past decade, unintentional ocular injury during surgery may still occur. Following such trauma, inflammatory mediators such as PGs and the enzymes COX-1 and COX-2 become activated and are released [2]. These inflammatory mediators contribute to various ocular symptoms including pain, inflammation, miosis, posterior synechiae, posterior capsular opacification, changes in IOP and glaucoma [3].

Small-incision cataract surgery has become the standard of care for Extracapsular Cataract Extraction (ECCE), owing to major technical improvements in recent decades. However, the ocular tissues are traumatised during surgery, leading to activation of phospholipase A2 and the release of two major lipid molecules: Platelet-Activating Factors (PAFs) and metabolites of Arachidonic Acid (AA). The primary pathways that utilise AA as a substrate include the cyclo-oxygenase and lipoxygenase pathways. PGs and Leukotrienes (LTs) are the main byproducts of these pathways. Endogenous PGs contribute to increased conjunctival hyperaemia, altered IOP, increased blood-ocular barrier permeability, miosis during surgery and postoperative inflammation [4].

A reduction in pupil size increases the likelihood of complications, including surgical trauma, posterior capsule rupture and postoperative ocular inflammation, all of which can make cataract surgery more challenging [5,6]. Previous studies have shown that the likelihood of posterior capsule rupture is reduced by half when mydriasis exceeds 6 mm. Therefore, maintaining an adequate level of pupil dilation is considered essential for successful cataract extraction [7].

Macular oedema is one of the primary causes of poor visual outcomes following cataract surgery. Previous studies have reported that the incidence of phacoemulsification-induced clinical CMO may reach up to 2% [8]. Some studies have also noted an increase in foveal thickness detected using Optical Coherence Tomography (OCT) [9].

The NSAIDs such as nepafenac act by inhibiting COX, the enzyme responsible for producing Prostaglandins (PGs) that promote inflammation. The corneal epithelium is permeable to nepafenac

[10]. Its anti-inflammatory effect occurs following its conversion within the eye to the active metabolite, amfenac [11]. Amfenac itself cannot penetrate the corneal epithelium but is a potent inhibitor of PG synthesis, blocking both COX-1 and COX-2 [12]. Topical 0.1% nepafenac solution is highly effective in reducing postoperative pain and inflammation, as well as preventing intraoperative miosis [13]. Therefore, the purpose of this study is to evaluate the effectiveness of prophylactic topical nepafenac 0.1% in maintaining intraoperative mydriasis and preventing postoperative macular oedema during topical phacoemulsification cataract surgery.

Objectives

- To evaluate the effectiveness of prophylactic nepafenac in maintaining intraoperative mydriasis and preventing postoperative macular oedema.
- To evaluate the efficacy of standard antibiotic and corticosteroid therapy in maintaining intraoperative mydriasis and preventing postoperative macular oedema.
- To compare the efficacy of 0.1% nepafenac with standard antibiotic and corticosteroid therapy in maintaining intraoperative mydriasis and preventing postoperative macular oedema.

Null Hypothesis (H_0): There is no significant difference between 0.1% nepafenac and standard antibiotic plus corticosteroid therapy in maintaining intraoperative mydriasis and preventing postoperative macular oedema.

Alternate Hypothesis (H_1): There is a significant difference between 0.1% nepafenac and standard antibiotic plus corticosteroid therapy in maintaining intraoperative mydriasis and preventing postoperative macular oedema.

REVIEW OF LITERATURE

The risk of macular oedema after cataract surgery has been documented in several studies. Visual acuity–impairing CMO has been reported in 1% to 4% of cases [14]. In a study by Song SH et al., reduced visual acuity and macular oedema (central macular thickness >300 µm) were observed one month post-surgery in 1.02% of patients, which is consistent with previous incidence estimates [15].

Bromfenac is more selective for COX-2 than COX-1. Compared to other NSAIDs, bromfenac demonstrates a half-maximal inhibitory concentration of 0.0066–0.0075 µmol/L, making it up to four times more potent against COX-2 [15]. The presence of bromine in its chemical structure increases lipophilicity, enhancing corneal penetration, intraocular tissue absorption and vitreous concentration. Kim SJ et al., reported that bromination at position four of the phenyl ring prolongs its analgesic and anti-inflammatory activity [10]. Kida T et al., showed that bromfenac penetrates retinochoroidal tissues more effectively and remains in the retina longer than nepafenac, while Baklayan GA et al., found bromfenac superior to diclofenac, nepafenac and amfenac in this regard [16,17].

Several studies have shown that NSAIDs—either alone or in combination with steroid ophthalmic solutions—are more effective than steroids alone in reducing macular oedema following cataract surgery [18]. Evidence also suggests that NSAIDs should be added to postoperative steroid regimens in diabetic patients to prevent macular oedema [15].

This study aims to evaluate the effectiveness of prophylactic topical nepafenac 0.1% in maintaining intraoperative mydriasis and preventing postoperative macular oedema in patients undergoing topical phacoemulsification cataract surgery.

MATERIALS AND METHODS

A prospective, randomised, single-masked comparative study will be conducted in the Department of Ophthalmology at Acharya Vinoba Bhave Rural Hospital (AVBRH), Sawangi, Meghe, Maharashtra, India, from June 2024 to June 2026. Ethical approval has been obtained from the Institutional Ethics Committee (Ref: DMIHER(DU)/IEC/2024/23) and the study has been registered with the Clinical Trials Registry of India (CTRI) under the registration number CTRI/2025/05/087123.

Inclusion criteria:

- Adult patients aged 40 years or older.
- Diagnosis of senile and/or metabolic cataract.
- Scheduled for phacoemulsification surgery.
- Ability to comply with standard fundoscopy evaluation.

Exclusion criteria:

- Pregnant or nursing women.
- Any previous history of viral or inflammatory ocular disease, or treatment for ocular infection within 30 days prior to the study.
- History of ocular trauma or prior ocular surgery.
- Known allergy or hypersensitivity to study medications, preservatives, steroids, or other components; use of any ocular medications or systemic/topical steroids within 30 days before study initiation.
- Uncontrolled diabetes mellitus, proliferative diabetic retinopathy, or blood glucose level ≥126 mg/dL.
- Preoperative mydriasis <6 mm, presence of synechiae, or use of contact lenses in the study eye.

Sample size calculation: Sample size was calculated using the formula for mean difference.

$$n \geq z_{1-\frac{\alpha}{2}}(z1-\beta)2\sigma^2 \; {}_{1+\frac{\sigma^2}{r}/(\mu_1-\mu_2)^2}$$

where,

Alpha $\alpha = 0.01$

Beta $\beta = 0.1$

Mean in group $\mu 1 = 6.84$

Standard deviation in group $\sigma 1 = 0.93$

Mean in group $\mu 2 = 7.91$

Standard deviation in group $\sigma 1 = 0.74$ [19]

The calculated sample size was 18.35~ 19 per group

Participants will be allocated to the two groups using simple random sampling, conducted by the primary investigator. Prior to surgery, every patient will undergo a comprehensive ophthalmic evaluation along with a review of their medical history and current medications.

Study Procedure

Before surgery, each patient will undergo an ocular examination that includes Best-corrected Visual Acuity (BCVA) using the Snellen chart, a three-step magnification slit-lamp examination (Appasamy AIA-11), Intraocular Pressure (IOP) measurement using NIDEK non contact tonometry, fundus examination and macular OCT.

For topical mydriasis, both treatment groups will receive a single drop each of tropicamide 0.8% and phenylephrine 5%, administered every 15 minutes for two doses. Before the commencement of surgery, the study group will receive four doses of 0.1% nepafenac, one drop every 15 minutes. The control group will receive only prednisolone and moxifloxacin drops for a 15-day taper.

The surgeons will remain unaware of whether a patient has received preoperative mydriatics alone or in combination with nepafenac. All cataract surgeries will be performed by a single surgeon using phacoemulsification with Intraocular Lens (IOL) implantation within the capsular bag. A standardised small-incision phacoemulsification technique will be used for all patients.

A 5.0 mm capsulorhexis will be created, followed by 1.0 mm nasal and 2.8 mm temporal clear corneal incisions [19]. Foldable IOLs will be implanted in the capsular bag using a prechopped phacoemulsification technique. No sutures will be required to seal the corneal incisions. Phacoemulsification parameters will be standardised before each procedure and kept consistent across all cases.

The Infiniti® Vision System with Ozil technology (Alcon Laboratories, Inc.) will be used for all surgeries. The pre-set parameters will include: amplitude = 100%; irrigation with balanced, adrenaline-free saline solution; bottle height = 110 cm; aspiration flow rate = 38 mL/min; vacuum pressure = 350 mmHg; and dynamic rise = 1.

Vertical and horizontal pupil diameters will be measured in millimetres using a compass under the operating microscope at four key time points: before surgery, after nuclear emulsification, following cortical aspiration and postoperatively. The microscope's standard magnification will be maintained consistently for all four measurements.

Postoperatively, all patients will receive topical antibiotic–corticosteroid therapy (moxifloxacin + prednisolone) hourly for 15 days, followed by a 4-week tapering schedule.

Outcomes

A Fast Macular Thickness Map scan will be used to assess foveal thickness (FT, central 1 mm) in microns and total macular volume (TMV) in mm^3. This scan will also aid in detecting structural macular changes.

Intraocular Pressure (IOP) will be measured using NIDEK's non contact tonometer, which uses a gentle puff of air to applanate the cornea without direct contact.

For the fundus examination, patients will be placed in a dimly lit room and asked to fixate on a distant target. The ophthalmoscope will be positioned against the patient's cheek and they will be instructed to look through the device. Fundus photography will be used to assess fundus condition and identify any abnormalities.

Macular OCT will generate high-resolution, three-dimensional images of the retina. By scanning a laser beam across the retina, OCT will provide detailed visualisation of retinal layers and may also reveal the structure of the optic nerve. The patient will be seated in front of the OCT device during the scan, which will help detect any macular oedema.

After imaging is completed, dilating eye drops will be administered to enlarge the pupils, temporarily increasing light sensitivity.

All procedures will be performed preoperatively and at the 4th and 6th postoperative weeks.

STATISTICAL ANALYSIS

Data will be entered into a Microsoft Excel spreadsheet and all statistical analyses will be performed using Statistical Package for the Social Sciences (SPSS) software (version 28.0). Descriptive, subgroup and multivariate analytical models will be applied to identify variables associated with adverse outcomes. To assess the relationships between demographic, clinical and aetiological factors and outcome measures, the independent t-test, Fisher's-exact test for categorical variables and the Chi-square test will be used as appropriate.

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