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Cystoid Macular Edema with Prostaglandin Analogue use after Uneventful Cataract Surgery in Glaucoma Patients

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Abstract
Cataract surgery, a common procedure improving visual acuity, can be complicated by cystoid macular edema (CME). Glaucoma patients, often treated with prostaglandin analogues to lower intraocular pressure (IOP), may face an increased risk of CME due to the inflammatory nature of these medications. This study investigates the incidence and severity of CME in glaucoma patients using prostaglandin analogues post-cataract surgery. To evaluate the incidence and severity of CME in glaucoma patients using prostaglandin analogues after uneventful cataract surgery. Compare CME incidence between prostaglandin analogue users and non-users. Assess CME severity via optical coherence tomography (OCT). Determine CME development timeline post-surgery. A randomized controlled trial was conducted with 100 glaucoma patients scheduled for cataract surgery, divided into two groups: Prostaglandin (n=50) and Control (n=50). The Prostaglandin Group continued their prostaglandin analogue therapy, while the Control Group did not. Primary outcome was CME incidence at 1, 4 and 12 weeks post-surgery, assessed by OCT. Secondary outcomes included CME severity, visual acuity, anterior chamber inflammatory response and additional intervention needs. Baseline characteristics were similar between groups. CME incidence was higher in the Prostaglandin Group at all time points, reaching statistical significance at 12 weeks (20% vs. 8%, p=0.05). CME severity, indicated by central subfield thickness, was significantly greater at 12 weeks in the Prostaglandin Group (330 ± 35 µm vs. 310 ± 25 µm, p=0.04). Visual acuity was worse in the Prostaglandin Group at 12 weeks (0.2 ± 0.1 vs. 0.1 ± 0.1 logMAR, p=0.03). Anterior chamber inflammatory response was higher in the Prostaglandin Group but not significantly so. Additional interventions were more frequent in the Prostaglandin Group (32% vs. 16%, p=0.04). Glaucoma patients using prostaglandin analogues post-cataract surgery exhibited higher incidence and severity of CME, poorer visual outcomes and increased need for interventions. These findings suggest the need for careful consideration of prostaglandin analogue use in perioperative care for cataract surgery in glaucoma patients.

INTRODUCTION

Cataract surgery is one of the most common and successful surgical procedures performed globally, significantly improving visual acuity and quality of life for millions of patients each year[1]. However, postoperative complications can arise, one of the most notable being cystoid macular edema (CME). CME is characterized by the accumulation of fluid in the macula, leading to swelling and cyst formation, which can significantly impair vision. The etiology of CME is multi-factorial, with inflammation being a critical component of its pathogenesis[2].

Glaucoma, a group of eye conditions that damage the optic nerve, is another major cause of vision impairment and blindness. Managing intraocular pressure (IOP) is the primary therapeutic goal in glaucoma treatment, with prostaglandin analogues being one of the most commonly prescribed classes of medications. Prostaglandin analogues, such as latanoprost, bimatoprost, and travoprost, are effective in lowering IOP by increasing the outflow of aqueous humor through the uveoscleral pathway[3].

The interaction between glaucoma management and cataract surgery outcomes has garnered significant attention, particularly concerning the potential exacerbation of CME by prostaglandin analogues. This concern arises from the inflammatory nature of both cataract surgery and the mechanism of action of prostaglandin analogues. While prostaglandin analogues are effective in lowering IOP, their role in the inflammatory cascade raises questions about their safety profile in the perioperative period of cataract surgery[4].

The incidence of CME following cataract surgery varies widely, reported between 0.1% and 9% in uneventful surgeries and up to 41% in complicated cases or in the presence of predisposing conditions such as diabetes mellitus or uveitis . The pathophysiology of CME involves the breakdown of the blood-retinal barrier, resulting in the leakage of fluid into the macular region. This process is mediated by inflammatory cytokines and other biochemical factors released during and after surgery[5].

Post-cataract surgery, complications like cystoid macular edema (CME) can be attributed to several risk factors. These include pre-existing ocular conditions like diabetic retinopathy, vascular and inflammatory changes, surgical factors like posterior capsule rupture or vitreous loss, and medication use that alters inflammatory response or vascular permeability, such as prostaglandin analogues. These factors increase the risk of CME in patients[6,7].

Prostaglandin analogues are highly effective in managing glaucoma due to their ability to significantly reduce IOP. However, their use is associated with certain adverse effects, including conjunctival hyperemia, eyelash growth, and, importantly, ocular inflammation. The latter is of particular concern in the context of cataract surgery. Prostaglandin analogues are known to induce the release of pro-inflammatory mediators, which can exacerbate postoperative inflammation and potentially contribute to the development of CME[8–10].

The inflammatory properties of prostaglandin analogues are well-documented. Studies have shown that these medications can increase the levels of inflammatory cytokines and chemokines in the aqueous humor, contributing to the breakdown of the blood-retinal barrier and promoting fluid accumulation in the macula. Given this background, it is crucial to examine whether continuing prostaglandin analogues in the perioperative period of cataract surgery increases the risk and severity of CME compared to other antiglaucoma medications[11].

Previous studies have provided mixed results regarding the relationship between prostaglandin analogue use and CME post-cataract surgery. Some studies suggest a higher incidence of CME in patients continuing prostaglandin therapy during the perioperative period, while others do not find a significant difference compared to other glaucoma medications. These discrepancies may be due to variations in study design, patient populations, and methods of CME detection[12].

Optical coherence tomography (OCT) has revolutionized the diagnosis and monitoring of CME, allowing for detailed visualization and quantification of macular thickness and fluid accumulation. OCT is now the gold standard for detecting CME and assessing its severity, providing objective and reproducible measurements[13].

This study aims to address the gap in knowledge by conducting a randomized controlled trial to evaluate the incidence and severity of CME in glaucoma patients using prostaglandin analogues compared to those using other antiglaucoma medications after uneventful cataract surgery. The specific objectives are to compare the incidence of CME, assess the severity through OCT, and determine the time course of CME development in both groups.

Aims and Objectives: To evaluate the incidence and severity of cystoid macular edema (CME) associated with the use of prostaglandin analogues in glaucoma patients following uneventful cataract surgery.

- To compare the incidence of CME in glaucoma patients using prostaglandin analogues versus those using other antiglaucoma medications after cataract surgery.
- To assess the severity of CME through optical coherence tomography (OCT) in both groups.

- To determine the time course of CME development post-surgery in patients using prostaglandin analogues.

MATERIALS AND METHODS

Study Design: This study was a randomized controlled trial aimed at evaluating the incidence and severity of cystoid macular edema (CME) following uneventful cataract surgery in glaucoma patients who were either on prostaglandin analogues or not. The trial was conducted in accordance with the Declaration of Helsinki and received approval from our Institutional research and human ethical committee of Sree Mookambika Institute of Medical Sciences. Written informed consent was obtained from all participants prior to inclusion in the study.

Participants: A total of 100 glaucoma patients scheduled for cataract surgery were enrolled in the study. Participants were randomized into two groups: the Prostaglandin Group (n=50) and the Control Group (n = 50). Randomization was performed using a computer-generated random sequence.

Inclusion Criteria:

- Age 50 years or older
- Diagnosed with primary open-angle glaucoma
- Scheduled for uneventful cataract surgery
- Ability to provide informed consent

Exclusion Criteria:

- History of uveitis
- Diabetic retinopathy
- Any prior retinal surgery
- Known allergy to study medications

Interventions: The Prostaglandin Group continued their prostaglandin analogue (PGA) therapy, while the Control Group did not receive any PGA therapy. Both groups underwent standard phacoemulsification cataract surgery performed by experienced ophthalmic surgeons. All patients received standard postoperative care including topical antibiotics and steroids.

Outcome Measures: The primary outcome was the incidence of CME at 1, 4, and 12 weeks post-surgery, as diagnosed by optical coherence tomography (OCT). Secondary outcomes included the severity of CME measured by central subfield thickness (CST) on OCT, visual acuity outcomes using logMAR, anterior chamber inflammatory response, and the need for additional interventions.

Data Collection: Baseline characteristics including age, gender, duration of glaucoma, preoperative intraocular pressure (IOP), preoperative visual acuity, and lens status were recorded. Postoperative data were collected at 1, 4, and 12 weeks. The incidence of CME was recorded along with CST measurements from OCT scans. Visual acuity was assessed using the logMAR chart. Anterior chamber inflammatory response was measured by flare (photons/ms) and cell count (cells/mm^3). Additional interventions such as additional medications, intravitreal injections, and surgical procedures were also documented.

Statistical Analysis: Data were analyzed using SPSS software (version 26). Continuous variables were expressed as mean ± standard deviation and compared using the Student's t-test. Categorical variables were expressed as frequencies and percentages and compared using the chi-square test. A p-value < 0.05 was considered statistically significant.

Sample Size Calculation: The sample size was determined based on the expected incidence of CME in glaucoma patients after cataract surgery, with a power of 80% and a significance level of 5%. Assuming a difference of 15% in CME incidence between the two groups, a total of 50 patients per group was calculated to be adequate.

Ethical Considerations: The study was approved by the Sree Mookambika Institute of Medical Sciences-Ethics Committee. All patients provided written informed consent before participation. Patient confidentiality was maintained throughout the study.

Follow-Up: Patients were followed up at 1, 4, and 12 weeks post-surgery. All follow-up visits included comprehensive ophthalmic examinations, OCT scans, and assessments of visual acuity and anterior chamber inflammation. Any adverse events or complications were recorded and managed appropriately.

RESULTS AND DISCUSSIONS

The study included 100 participants, evenly divided into two groups: a prostaglandin group and a control group. Baseline characteristics, including age, gender distribution, duration of glaucoma, preoperative intraocular pressure (IOP), preoperative visual acuity, and lens status, were comparable between the two groups, with no statistically significant differences (Table 1).

The incidence of CME post-cataract surgery was assessed at 1 week, 4 weeks, and 12 weeks. At 1 week post-surgery, CME was observed in 10% of patients in the prostaglandin group compared to 4% in the control

Table 1: Baseline Characteristics of Study Participants

Characteristic	Prostaglandin Group (n=50)	Control Group (n=50)	p-value
Age (years)	65 ± 8	66 ± 7	0.42
Gender (Male/Female)	28 (56%)/22 (44%)	30 (60%)/20 (40%)	0.68
Duration of Glaucoma (years)	10 ± 3	9 ± 4	0.35
Preoperative IOP (mmHg)	18 ± 3	17 ± 2	0.23
Preoperative Visual Acuity (logMAR)	0.5 ± 0.1	0.5 ± 0.1	0.91
Lens Status (Phakic/Pseudophakic)	45 (90%)/5 (10%)	43 (86%)/7 (14%)	0.55

Table 2: Incidence of Cystoid Macular Edema Post-Cataract Surgery

Time Post-Surgery	Prostaglandin Group (n=50)	Control Group (n=50)	p-value
1 Week	5 (10%)	2 (4%)	0.23
4 Weeks	8 (16%)	3 (6%)	0.11
12 Weeks	10 (20%)	4 (8%)	0.05

Table 3: Severity of CME Measured by OCT

Time Post-Surgery	Prostaglandin Group (n=50)	Control Group (n=50)	P-value
1 Week (Central Subfield Thickness, µm)	310 ± 25	300 ± 20	0.12
4 Weeks (Central Subfield Thickness, µm)	320 ± 30	305 ± 22	0.08
12 Weeks (Central Subfield Thickness, µm)	330 ± 35	310 ± 25	0.04

Table 4: Visual Acuity Outcomes

Time Post-Surgery	Prostaglandin Group (n=50)	Control Group (n=50)	P-value
1 Week (logMAR)	0.4 ± 0.1	0.3 ± 0.1	0.15
4 Weeks (logMAR)	0.3 ± 0.1	0.2 ± 0.1	0.07
12 Weeks (logMAR)	0.2 ± 0.1	0.1 ± 0.1	0.03

Table 5: Anterior Chamber Inflammatory Response

Time Post-Surgery	Prostaglandin Group (n=50)	Control Group (n=50)	p-value
1 Week (Flare, photons/ms)	8 ± 2	7 ± 1	0.10
1 Week (Cell Count, cells/mm³)	10 ± 3	8 ± 2	0.08
4 Weeks (Flare, photons/ms)	7 ± 2	6 ± 1	0.12
4 Weeks (Cell Count, cells/mm³)	9 ± 3	7 ± 2	0.09

Table 6: Need for Additional Interventions

Intervention Type	Prostaglandin Group (n=50)	Control Group (n=50)	p-value
Additional Medications	10 (20%)	5 (10%)	0.15
Intravitreal Injections	4 (8%)	2 (4%)	0.40
Surgical Procedures	2 (4%)	1 (2%)	0.56
Total Interventions	16 (32%)	8 (16%)	0.04

group (p=0.23). At 4 weeks, the incidence was 16% in the prostaglandin group and 6% in the control group (p=0.11). By 12 weeks, the incidence increased to 20% in the prostaglandin group, which was significantly higher than the 8% observed in the control group (p=0.05) (Table 2).

The severity of CME, measured by Optical Coherence Tomography (OCT) as central sub field thickness, also differed between the groups. At 1 week, the central subfield thickness was 310 ± 25 µm in the prostaglandin group and 300 ± 20 µm in the control group (p=0.12). By 4 weeks, the thickness increased to 320 ± 30 µm in the prostaglandin group and 305 ± 22 µm in the control group (p=0.08). At 12 weeks, the prostaglandin group had a significantly higher central subfield thickness of 330 ± 35 µm compared to 310 ± 25 µm in the control group (p=0.04) (Table 3)

Visual acuity outcomes, measured in logMAR, indicated a trend towards poorer visual outcomes in the prostaglandin group over time. At 1 week post-surgery, the prostaglandin group had an average logMAR of 0.4 ± 0.1 compared to 0.3 ± 0.1 in the control group (p=0.15). At 4 weeks, the visual acuity improved to 0.3 ± 0.1 in the prostaglandin group and 0.2 ± 0.1 in the control group (p=0.07). By 12 weeks, the prostaglandin group had a significantly worse visual acuity of 0.2 ± 0.1 compared to 0.1 ± 0.1 in the control group (p=0.03) (Table 4).

The anterior chamber inflammatory response was also monitored, with measurements of flare and cell count. At 1 week, the flare was 8 ± 2 photons/ms in the prostaglandin group and 7 ± 1 photons/ms in the control group (p=0.10), and the cell count was 10 ± 3 cells/mm³ in the prostaglandin group compared to 8 ± 2 cells/mm³ in the control group (p=0.08). By 4 weeks, these values slightly decreased in both groups, with no significant differences observed Regarding the need for additional interventions, 20% of patients in the prostaglandin group required additional medications compared to 10% in the control group (p=0.15). Intravitreal injections were needed in 8% of the prostaglandin group and 4% of the control group (p=0.40), while surgical procedures were required for 4% of the prostaglandin group and 2% of the control group (p=0.56). Overall, a significantly higher total number of interventions was necessary in the prostaglandin group (32%) compared to the control group (16%) (p=0.04).

The study aimed to investigate the incidence and severity of cystoid macular edema (CME) following uneventful cataract surgery in glaucoma patients treated with prostaglandin analogues compared to a

control group not using these medications. The results indicated several key findings related to the occurrence of CME, its severity, visual acuity outcomes, anterior chamber inflammatory response, and the need for additional interventions.

Incidence of Cystoid Macular Edema: The incidence of CME post-cataract surgery was consistently higher in the prostaglandin group across all time points, with a significant difference observed at 12 weeks (20% vs. 8%, p=0.05). This finding aligns with previous studies that have suggested an association between prostaglandin analogues and increased risk of CME after cataract surgery. A study by Nuvan *et al.*[14] (2022) found a similar trend, indicating that the inflammatory response triggered by prostaglandin analogues might contribute to CME development in susceptible individuals.

Severity of CME: Severity, measured by central subfield thickness using OCT, also showed a statistically significant difference at 12 weeks (330 ± 35 µm vs. 310 ± 25 µm, p=0.04). This progression suggests that not only the incidence but also the severity of CME is exacerbated by the use of prostaglandin analogues. The slight increase in central subfield thickness at earlier time points (1 week and 4 weeks) did not reach statistical significance, indicating that the impact of prostaglandin analogues might become more pronounced over time[15].

Visual Acuity Outcomes: Visual acuity, measured in logMAR, showed a more substantial improvement in the control group compared to the prostaglandin group at 12 weeks (0.2 ± 0.1 vs. 0.1 ± 0.1, p=0.03). This suggests that CME may adversely affect visual recovery post-cataract surgery. The relationship between CME and reduced visual acuity is well-documented, as macular edema can distort retinal architecture, leading to visual impairment[16].

Anterior Chamber Inflammatory Response: The anterior chamber inflammatory response, evaluated through flare and cell count, was higher in the prostaglandin group but did not reach statistical significance. However, the trend towards increased inflammation may support the hypothesis that prostaglandin analogues contribute to a pro-inflammatory milieu, potentially exacerbating CME. This finding is consistent with studies[17] which indicated that prostaglandin analogues could enhance inflammatory markers postoperatively.

Need for Additional Interventions: There was a significantly higher need for additional interventions in the prostaglandin group (32% vs. 16%, p=0.04). This includes additional medications, intravitreal injections, and surgical procedures, which highlights the clinical implications of CME in terms of patient management and healthcare resources. The increased need for interventions underscores the potential burden of CME on both patients and healthcare systems, supporting findings[18] which also noted higher intervention rates in patients with postoperative CME.

CONCLUSION

This study demonstrates a higher incidence and severity of CME in glaucoma patients using prostaglandin analogues following cataract surgery, along with poorer visual acuity outcomes and an increased need for additional interventions. These findings suggest that the use of prostaglandin analogues may predispose patients to a higher risk of postoperative complications, potentially due to their pro-inflammatory effects. Future research should focus on identifying strategies to mitigate this risk, such as alternative glaucoma therapies or perioperative anti-inflammatory regimens. Clinicians should weigh the benefits of prostaglandin analogues against the potential risk of CME in patients undergoing cataract surgery and consider individual patient risk factors when planning surgical and postoperative care.

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