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Original Research Article

Comparison of Pre- and Post-Operative Administration of Oral Carbonic Anhydrase Inhibitors Versus No Administration of Oral Carbonic Anhydrase Inhibitors in Patients Undergoing Cataract Surgery

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Abstract:

Background: Increased intraocular pressure (IOP) after cataract surgery is a major frequent short-term complication of Cataract Surgery. Although oral carbonic anhydrase inhibitors (CAIs) are known to lower intraocular pressure (IOP), research is still ongoing to determine the best time to administer them.

Objective: To compare the efficacy of preoperative versus postoperative oral CAI administration in preventing postoperative IOP elevation following cataract surgery.

Methods: A prospective randomized controlled trial was conducted at Zoram Medical College and Hospital, Mizoram, over 2 years, involving 200 patients undergoing Small Incision Cataract surgery (SICS). Patients were randomized into three groups: Group A (preoperative CAI), Group B (postoperative CAI), and Group C (control, no CAI). IOP was measured preoperatively and at 1 hour, 6 hours, 24 hours, and 1 week postoperatively. Primary outcome was the incidence and magnitude of postoperative IOP rise; secondary outcomes included systemic/ocular adverse effects.

Results: At 1 hour postoperatively, mean IOP was significantly lower in Group A (18.6 ± 2.5 mmHg) compared to Group B (21.5 ± 2.7 mmHg) and Group C (24.8 ± 3.2 mmHg) ($p < 0.001$). IOP spikes >30 mmHg occurred in 18% of controls, 6% of postoperative CAI patients, and 1.5% of preoperative CAI patients. By 1 week, IOP normalized in all groups. Mild adverse effects such as paresthesia and fatigue were noted but were self-limiting.

Conclusion: Preoperative CAI administration provides superior prophylaxis against acute postoperative IOP elevation compared to postoperative dosing or no treatment. It should be considered as part of routine perioperative management in cataract surgery, especially in high-risk patients.

Keywords: Cataract surgery; carbonic anhydrase inhibitors; acetazolamide; postoperative complications; small incision cataract surgery.

Introduction

Cataract surgery is one of the most commonly performed ophthalmic procedures worldwide and remains the definitive treatment for cataract, which continues to be a leading cause of avoidable blindness [1]. Despite improvements in surgical techniques, one persistent challenge is the transient rise in intraocular pressure (IOP) during the early postoperative period [2]. Although most patients tolerate this increase, individuals with glaucoma, compromised optic nerves, or ocular hypertension are at risk of visual deterioration [3].

To prevent these IOP spikes, various strategies are employed, including thorough viscoelastic removal, topical pressure-lowering agents, and systemic medications [4]. Among these, oral carbonic anhydrase inhibitors (CAIs) such as acetazolamide are well established for their ability to suppress aqueous humor formation and reduce IOP [5]. Their rapid onset of action has made them useful in both acute and chronic glaucoma management, as well as in the perioperative setting [6].

Previous trials have suggested that preoperative administration of acetazolamide may be more

effective than postoperative dosing in preventing IOP surges [3]. In eyes with pseudoexfoliation or pre-existing glaucoma, preoperative acetazolamide has shown particular benefit [7]. However, some studies have reported minimal differences between treated and untreated groups, raising questions about the necessity of routine systemic prophylaxis, particularly given the risk of side effects such as paresthesia, fatigue, gastrointestinal upset, and, rarely, metabolic acidosis or renal complications [5,8].

Given these conflicting findings, further evidence is required to clarify the role of perioperative oral CAIs in modern cataract surgery. This randomized controlled trial, conducted at Zoram Medical College & Hospital, Mizoram, aims to compare preoperative and postoperative administration of oral carbonic anhydrase inhibitors with no administration, in order to evaluate their efficacy in reducing postoperative IOP spikes and to assess related safety outcomes.

Materials and Methods

Study Design: Over the course of two years (2023–2025), this study was carried out at the Department of Ophthalmology, Zoram Medical College & Hospital, Mizoram, as a preliminary, randomized, controlled trial.

Study Population and Sample Size: A total of 200 patients scheduled to undergo small incicion cataract surgery with posterior chamber intraocular lens implantation were enrolled. Sample size was determined based on previous studies evaluating the effect of oral carbonic anhydrase inhibitors (CAIs) on postoperative intraocular pressure (IOP), assuming a 95% confidence level and 80% statistical power.

Inclusion Criteria

- Patients aged 40–80 years undergoing elective cataract surgery
- Clear corneal SICS candidates with posterior chamber intraocular lens implantation
- Patients willing to provide in written approval

Exclusion Criteria

- Pre-existing glaucoma or ocular hypertension requiring topical/systemic anti-glaucoma therapy
- History of intraocular surgery or trauma
- Ocular comorbidities such as pseudoexfoliation, uveitis, or retinal disease
- Known hypersensitivity to sulfonamides or carbonic anhydrase inhibitors
- Systemic contraindications to acetazolamide (e.g., renal/hepatic impairment, metabolic acidosis)

Randomization and Group Allocation: The patients were randomly assigned to three groups (n = ~67 each group) using a digital stream of randomly generated numbers:

Group A (Preoperative CAI group): Received oral acetazolamide 250 mg, two hours before surgery.

Group B (Postoperative CAI group): Received oral acetazolamide 250 mg immediately after surgery.

Group C (Control group): Did not receive any systemic CAI.

All patients underwent Small Incision Cataract surgery by experienced surgeons using uniform technique and viscoelastic removal protocol.

Outcome Measures

The primary outcome was the change in intraocular pressure (IOP) postoperatively. IOP was measured using Goldmann applanation tonometry at the following time points:

- Baseline (preoperative)
- 1 hour postoperatively
- 6 hours postoperatively
- 24 hours postoperatively
- 1 week postoperatively

The secondary outcomes included:

- Incidence of significant IOP spikes (>30 mmHg)
- Ocular complications (corneal edema, anterior chamber inflammation)
- Systemic adverse effects of acetazolamide (paresthesia, fatigue, gastrointestinal upset, electrolyte disturbances)

Statistical Analysis: SPSS version 26.0 was used to enter and analyze the data (IBM Corp., Armonk, NY, USA). Analysis of variance (ANOVA) with post-hoc testing when necessary was used to compare continuous variables, which were reported as mean ± standard deviation. The Chi-square test was used to assess categorical variables, which were represented as frequencies and percentages. Statistical significance is characterized as a p-value of less than 0.05.

Ethical Considerations: The Institutional Ethics Committee of Zoram Medical College and Hospital in Mizoram gave its approval to the work. All subjects gave their written informed consent prior to enrollment. The study complied with the 2013 edition of the Declaration of Helsinki.

Result

Baseline Characteristics: Group A (Pre-op CAI, n = 67), Group B (Post-op CAI, n = 66), and Group C (Control, n = 67) comprised the three randomly

assigned groups of 100 patients. Participants' ages ranged from 45 to 79 years old, with a mean age of 62.1 ± 7.5 years. There was no significant difference in age across groups (p = 0.84). Systemic comorbidities (diabetes mellitus 24 percent, hypertension 31 percent) and gender distribution (male 52 percent, female 48 percent) were also similar between groups (p > 0.05). Group A's mean baseline IOP was 15.2 ± 2.0 mmHg, Group B's was 15.4 ± 2.1 mmHg, and Group C's was 15.3 ± 2.3 mmHg; p = 0.93.

Table 1: Baseline demographic and clinical characteristics of study participants

Variable	Group A (n=67)	Group B (n=66)	Group C (n=67)	p-value
Age (years, mean ± SD)	62.4 ± 7.6	61.7 ± 7.3	62.1 ± 7.7	0.84
Male (%)	52.2	50.0	53.7	0.91
Diabetes Mellitus (%)	25.4	22.7	23.9	0.89
Hypertension (%)	31.3	30.3	32.8	0.95
Baseline IOP (mmHg)	15.2 ± 2.0	15.4 ± 2.1	15.3 ± 2.3	0.93

Intraocular Pressure (IOP) Changes: Postoperative IOP rose significantly in the control group compared with both intervention groups.

1 hour post-op: Group C (Control) demonstrated the highest mean IOP (24.8 ± 3.2 mmHg), while Group A (Pre-op CAI) had the lowest (18.6 ± 2.5 mmHg). Group B (Post-op CAI) showed intermediate values (21.4 ± 2.9 mmHg). The intergroup difference was statistically significant (p < 0.001).

6 hours post-op: Group A maintained lower IOP (17.9 ± 2.4 mmHg) compared with Group B (19.8 ± 2.6 mmHg) and Group C (22.2 ± 2.7 mmHg) (p < 0.001).

24 hours post-op: Group A (16.2 ± 2.3 mmHg) and Group B (16.8 ± 2.1 mmHg) had comparable values, both significantly lower than Group C (18.9 ± 2.5 mmHg) (p = 0.002).

1 week post-op: IOP values normalized across all groups (p = 0.27).

Table 2. Comparison of mean IOP values across groups

Time Interval	Group A (Pre-op CAI)	Group B (Post-op CAI)	Group C (Control)	p-value
Baseline	15.2 ± 2.0	15.4 ± 2.1	15.3 ± 2.3	0.93
1 hour post-op	18.6 ± 2.5	21.4 ± 2.9	24.8 ± 3.2	<0.001
6 hours post-op	17.9 ± 2.4	19.8 ± 2.6	22.2 ± 2.7	<0.001
24 hours post-op	16.2 ± 2.3	16.8 ± 2.1	18.9 ± 2.5	0.002
1 week post-op	15.1 ± 1.9	15.3 ± 2.0	15.6 ± 2.1	0.27

Incidence of IOP Spikes: Significant postoperative IOP spikes (>30 mmHg) were observed in:

Group A: 1/67 patients (1.5%)

Group B: 3/66 patients (4.5%)

Group C: 12/67 patients (17.9%)

The difference among groups was statistically significant (p < 0.001).

Ocular and Systemic Adverse Effects

Ocular: Mild corneal edema was seen in 3 patients (Group A: 1, Group B: 1, Group C: 1). Anterior chamber inflammation (mild) occurred in 2 patients (Group C). No sight-threatening complications were observed.

Systemic: Paresthesia and mild fatigue were reported in 7 patients (Group A: 4, Group B: 3). Gastrointestinal discomfort occurred in 3 patients (Group A: 2, Group B: 1). No patient required discontinuation of acetazolamide.

Table 3. Adverse ocular and systemic events

Adverse Event	Group A (n=67)	Group B (n=66)	Group C (n=67)
Corneal edema	1	1	1
Anterior chamber reaction	0	0	2
Paresthesia/fatigue	4	3	0
GI upset	2	1	0

Finally, the results can be summarized that the preoperative CAI significantly reduced immediate postoperative IOP rise compared with postoperative dosing and control. Postoperative CAI provided partial benefit but was less effective than preoperative administration. Control patients had the highest incidence of IOP spikes whereas adverse effects of acetazolamide were mild, transient, and did not necessitate withdrawal.

Discussion

The present randomized controlled trial evaluated the efficacy of preoperative versus postoperative administration of oral carbonic anhydrase inhibitors (CAIs) in controlling intraocular pressure (IOP) following cataract surgery. Our findings demonstrate that preoperative CAI use is more effective in attenuating the immediate postoperative IOP rise compared to postoperative administration and control. These results highlight the importance of timing in prophylactic IOP management among patients undergoing Small Incision cataract surgery

Postoperative IOP elevation is a well-documented phenomenon following cataract extraction, with reported incidence ranging from 18% to 45% depending on surgical technique and patient risk profile [9]. The etiology is multifactorial, involving retained viscoelastic material, inflammatory debris, and compromised aqueous outflow in the early postoperative period [10]. In our study, the control group exhibited a significant IOP rise at 1 hour postoperatively (mean 24.8 ± 3.2 mmHg), consistent with prior reports [11].

The administration of oral acetazolamide preoperatively significantly blunted this IOP rise, with mean values of 18.6 ± 2.5 mmHg at 1 hour and 17.9 ± 2.4 mmHg at 6 hours. This aligns with the findings of Thomas et al. [12], who observed that prophylactic pre-op acetazolamide resulted in a 40–60% reduction in immediate postoperative IOP spikes compared to untreated patients. Conversely, postoperative dosing in our study provided only partial benefit, with intermediate IOP values between pre-op and control groups, suggesting that the pharmacokinetic profile of CAIs is optimized when administered before surgery.

IOP spikes above 30 mmHg were observed in nearly 18% of control patients, while only 1.5% of pre-op CAI patients developed such events. This corroborates with studies by Shingleton et al. [2] and Lee et al. [13], both of which identified preoperative acetazolamide as a protective factor against sight-threatening IOP spikes in susceptible populations, particularly glaucoma patients. Although our cohort excluded patients with established glaucoma, the findings remain clinically relevant given that transient IOP rises may still compromise optic nerve health in borderline eyes.

Adverse effects were mild and transient in our study, with paresthesia, fatigue, and mild gastrointestinal upset being the most commonly reported symptoms. No patients discontinued therapy due to intolerance. Similar tolerability profiles have been reported in previous trials [14,15]. Importantly, no serious ocular or systemic complications were encountered, further supporting the short-term safety of CAI prophylaxis in cataract surgery.

The normalization of IOP across all groups by the first postoperative week indicates that the benefit of CAIs is primarily in the immediate perioperative period. Therefore, the clinical utility of CAIs lies in preventing acute IOP spikes rather than in long-term IOP management, consistent with previous evidence [16].

Strengths and Limitations: The strengths of this trial include its randomized controlled design, adequate sample size, and standardized surgical protocol. However, limitations must be acknowledged. The study was conducted in a single Medical College, which may affect generalizability. Additionally, while short-term IOP control was assessed, long-term outcomes such as endothelial cell count or visual field changes were not studied. Future multicentric trials with extended follow-up are warranted.

Clinical Implications: Our results suggest that preoperative administration of oral CAIs should be considered in routine cataract surgery, particularly in patients at risk of postoperative IOP elevation. This approach offers superior prophylaxis compared to postoperative dosing and carries minimal risk of significant adverse effects.

Conclusion

This randomized controlled trial demonstrated that preoperative administration of oral carbonic anhydrase inhibitors (CAIs) is significantly more effective than postoperative administration or no treatment in preventing acute intraocular pressure (IOP) spikes following cataract surgery. The prophylactic benefit was most evident in the first 6–12 hours postoperatively, with IOP levels stabilizing across all groups by the first postoperative week. Adverse effects were minimal and well tolerated. These findings support the use of preoperative CAIs as a safe and effective strategy to mitigate early postoperative IOP elevation, particularly in patients at risk of pressure-related complications.

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