

# Oral versus topical carbonic anhydrase inhibitors in ocular hypertension after scleral tunnel cataract surgery

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**Purpose:** To compare the effect of oral acetazolamide and topical 2% dorzolamide in prevention of ocular hypertension after scleral tunnel cataract surgery.

**Setting:** Ophthalmic department, Sana'a University, Yemen Sana'a from March 2007 to October 2007.

**Methods:** This prospective double-blind, randomized study included 150 eyes undergoing scleral tunnel cataract surgery with hard posterior chamber intraocular implantation. Methylcellulose was used as the viscoelastic in all surgery cases. Patients were assigned to one of three groups: group 1: topical gentamicin eye drops (control; n = 52); group 2: systemic acetazolamide 250 mg (n = 45); and group 3: topical 2% dorzolamide (n = 53). Acetazolamide patients received one 250 mg tablet, one hour before surgery, then half a tablet every eight hours. A topical dorzolamide 2% or gentamicin was applied in one drop one hour before surgery then every eight hours, for three days postoperatively. Intraocular pressures (IOP) were measured by Goldman applanation tonometry one hour preoperatively and 16, 24, and 48 hours postoperatively.

**Results:** At 16 hours, IOP between the three groups increased significantly with a statistically significant p-value of 0.008, but the mean IOP of acetazolamide patients was less than other groups. IOP nearly returned to the normal level 24 and 48 hours postoperatively, but this was not statistically significant (p = 0.452 and 0.138, respectively).

**Conclusion:** Acetazolamide offers better IOP control than topical dorzolamide 2% in preventing ocular hypertension after scleral tunnel cataract surgery.

**Keywords:** cataract surgery, ocular hypertension, viscoelastic, dorzolamide, intraocular pressure

## Introduction

A major reason for subsequent day assessment is to detect raised intraocular pressure (IOP), which complicates almost 8% of all cataract extractions.<sup>1</sup> Postoperative IOP increase is the most frequent short-term complication of cataract surgery.<sup>2-4</sup> It has become a major concern as an increasing number of cataract patients are having surgery in an outpatient setting and are discharged soon after surgery. Increasing demand for cataract surgery is resulting in a greater emphasis on high volume day-case procedures, where postoperative care varies widely from center to center, with little evidence-based practice. It is common for patients to be routinely assessed on the day after surgery, necessitating a further hospital visit.<sup>5,6</sup>

Postoperative assessment on the day of surgery will detect not only a spike of IOP, but also most early surgically related complications such as wound leak, iris prolapse, and a dislocated intraocular lens (IOL). Viscoelastic substances are widely used in small incision cataract surgery with several advantages. It has the maintenance of the anterior

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chamber space, protection of the corneal endothelium, and facilitation of the surgical procedure, especially during anterior capsulotomy and IOL implantation. It has some disadvantage of causing an increase in IOP within the first 24 hours after cataract surgery.<sup>7–16</sup> However, in small-incision cataract surgery there are occasional spikes of 30 mmHg or higher with the use of sodium hyaluronate.<sup>17</sup> Chakraborty and colleagues recommended the routine use of oral acetazolamide after phacoemulsification.<sup>18</sup> Systemic carbonic anhydrase inhibitors (CAIs) are associated with adverse effects such as acid-base disturbance, hypersensitivity reactions, and fatal aplastic anemia.<sup>11,19–21</sup>

We report a prospective double-blind randomized study where acetazolamide was given in select patients as a prophylactic IOP-lowering treatment after manual sutureless scleral tunnel cataract surgery with posterior chamber intraocular lens (PC IOL) implantation.

## Patients and methods

This prospective double-blind randomized study comprised 150 eyes from 150 consecutive patients (68 males and 82 females) with unilateral uncomplicated age-related cataract. All patients were scheduled for manual sutureless scleral tunnel cataract surgery with poly(methyl methacrylate) (PMMA) hard posterior chamber IOL implantation. Exclusion criteria included patients with history of glaucoma or lens-induced glaucoma and ocular hypertension more than 25 mmHg. Patients presenting with IOP less than 10 mmHg were excluded. Patients with uveitis, subluxating or dislocating crystalline lens, or previous ocular surgery or laser treatment were not involved in this study. Intraoperative posterior capsule rupture or vitreous loss was eliminated from the study. All patients with age-related cataract including hypermature and pseudoexfoliation syndrome with cataract were included in this study.

The preoperative baseline IOP was measured before using dilating drops, then Goldmann applanation tonometry one hour before surgery. Patients were randomly assigned to one of three groups based on the type of IOP-lowering medication given at one hour before surgery: group 1: one drop of gentamicin (control eyes); group 2: one tablet of acetazolamide (Cidamex) 250 mg; group 3: one drop of dorzolamide 2% (Xola) instead of apraclonidine due to its unavailability in the Yemen market. The ophthalmic nurse in our study was the only one to know which group received one of the three types of medications one hour before surgery immediately after taking the base IOP. All patients were operated on in the same fashion by the same consultant ophthalmologist. Dilating drops

(phenylephrine 2.5%, tropicamide 0.5%) were instilled in the operated eye approximately one to two hours before surgery. At the time of this study, phacoemulsification was not started yet and extracapsular cataract surgery with PC IOL was the standard technique for cataract surgery in our department.

Peribulbar anesthesia of lidocaine hydrochloride 2% was used in all cases. The operated eye was sterilized with povidone–iodine 5% solution for two minutes. After peribulbar anesthesia was administered, a fornix-based conjunctival flap was done, followed by adequate electrocautery for homeostasis, and then a 6 to 7 mm scleral tunnel incision curving away from the limbus “frown” incision from 11 o’clock to 1 o’clock position was performed by the same surgeon. Another temporal 2-mm corneal tunnel paracentesis incision was applied. The viscoelastic (methylcellulose) substance was injected into the anterior chamber. This was followed by capsulorrhexis, hydrodissection, and prolapse of the nucleus into the anterior chamber. Delivery of the nucleus using irrigating victus was followed by irrigation aspiration of the cortical materials remnants and cleaning of the capsular bag using Ringer’s lactate solution. The anterior chamber and capsular bag was expanded with the viscoelastic substance and a hard PMMA IOL implanted in the capsular bag. The viscoelastic substance was aspirated from the anterior chamber using an irrigation/aspiration (I/A) cannula. The incision was left sutureless while the conjunctiva was closed by electrocautery. No miotic agent was used intracamerally for all surgical patients. Capsule rupture did not occur in all cases. After surgery, the eye was patched after subconjunctival injection of gentamicin–dexamethasone.

After this, ophthalmic assistance was the administration of antiglaucoma drugs according to the subdivision of the patients, control group (gentamicin) eyedrops every eight hours, the second group received acetazolamide 250 mg half tablet every eight hours, while the third group received topical dorzolamide 2% (Xola) eyedrops every eight hours.

After 16 + 2 hours visits, dexamethasone 1% eye drops were used five times a day, then followed by measuring the IOP at 16, 24, and 48 hours after surgery. The IOP in the operated eye was measured by an ophthalmic resident unaware of the patient's group assignment using a Goldmann applanation tonometer.

The SPSS program (version 13; SPSS Inc., Chicago, IL, USA) was used to analyze the data of this study. Group comparisons of mean with standard deviation were associated with P-value in preoperative and postoperative IOP using a one-way ANOVA test. The mean IOP involving the standard deviation changes from preoperatively to 16 hours, and 24 to

48 hours postoperatively were calculated by paired sample *t*-test. The preoperative P value was compared to those after 16, 24, and 48 hours in each group by ANOVA tests.

## Results

This study includes 150 eyes from 150 patients who had surgery between March 2007 and October 2007. All patients were Yemeni in origin. All surgeries were completed by one consultant ophthalmologist without intraoperative complications.

The mean age was almost equal in all groups with a male-to-female ratio of 26:26 in the control group, 18:27 in the acetazolamide group, and 24:29 in the dorzolamide group (Table 1).

Table 2 shows the mean preoperative and postoperative IOP which peaked at 16 hours in all three groups and returned to nearly preoperative values by 48 hours. The mean IOP preoperatively was significantly lower in the dorzolamide group when compared between and within groups ( $p = 0.035$ ). Sixteen hours postoperatively, the mean IOP was significantly lower in the acetazolamide group than in the control and dorzolamide groups, respectively, while within groups highly statistically significant ( $p = 0.008$ ). At 24 and 48 hours IOP within groups ( $p = 0.452$  and  $0.138$ , respectively) returned to nearly basal IOP.

The mean difference in IOP changes from preoperatively to 16 hours, and 24 to 48 hours, postoperatively is shown in Table 3. The mean difference in IOP was almost equal in all groups without significant difference. At 24 and 48 hours, the mean IOP went down in all groups with no significant difference between groups.

Six (11.4%) control patients had an IOP of  $>30$  mmHg or higher at 16 hours compared with seven (12.3%) dorzolamide patients and only one (2.2%) acetazolamide patient. All of those patients with a previous diagnosis did not have glaucoma or ocular hypertension in the operated eye.

## Discussion

We found in this study that acetazolamide controls the rising IOP in the first 48 hours of manual sutureless scleral tunnel

cataract surgery with hard posterior chamber PMMA IOL implantation. IOP usually starts to rise two to four hours after surgery and lasts up to 24 hours, when most of the viscoelastic material has left the anterior chamber through the outflow channels.<sup>19-21</sup> Some studies assessing the frequency of a clinically significant elevation in IOP after cataract surgery found IOP to be transiently raised in 2.3% to 8.9% of cases.<sup>19,22</sup> Some causes contributing to elevated IOP after cataract surgery such as use of viscoelastic material<sup>23</sup> and retained lens matter may also cause uveitis and shooting of IOP after surgery. Prostaglandin releases after cataract surgery also play a role in elevated IOP.<sup>19-22,24,25</sup> Postoperative hyphema may occasionally cause an increased IOP by red blood cell blockage of the trabecular meshwork. Postoperative increase in IOP may be associated with pain, corneal edema, optic nerve damage, and visual field loss in patients with pre-existing glaucoma. Various drugs, including the systemic CAIs, timolol, pilocarpine gel, intracameral acetylcholine, and carbachol have been studied as agents to prevent postoperative IOP spikes.<sup>24-31</sup>

One of the primary functions of the next-day review visit is to measure and treat significantly raised IOP. Discharging patients a few hours after surgery may miss several patient guidelines. Many patients at risk of significant morbidity from a persistently raised postoperative IOP may not be detected otherwise. A lot of studies done in this field so far have been to detect and treat early shooting of IOP postoperatively.

In this study, we found that the IOP peaked after 16 hours postoperatively in the control ( $p = 0.000$ ) and dorzolamide groups ( $p = 0.000$ ), and acetazolamide patients had a statistically insignificant increase ( $p = 0.288$ ), while IOP increased statistically significantly between groups ( $p = 0.008$ ). This agrees with earlier studies in patients after extracapsular surgery in which IOP peaked six to eight hours postoperatively.<sup>32-35</sup> There were a few patients in the control and dorzolamide groups whose IOP levels reached up to 40 mmHg during the first 16 hours and returned to preoperative levels by 48 hours. Conversely, there were two (3.8%) patients from the dorzolamide group and only one (1.9%) patient in the control group whose IOP was lower than 5 mmHg 16 hours postoperatively. Close examination of these cases revealed deep anterior chambers and no wound leak. Significantly, the IOP returned to normal after 48 hours postoperatively and no complications were reported. This finding may represent suboptimal anterior chamber inflation at the conclusion of surgery<sup>36</sup> or ciliary body shutdown secondary to the peribulbar anesthesia.

**Table 1** Patient characteristics

Character	Control group	Acetazolamide group	Dorzolamide group
No of eyes	52	45	53
Mean age (years)	63.05 ± 9.53	60.15 ± 12.08	63.88
Age range (years)	46	59	55
Sex (M:F)	26:26	18:27	24:29

**Notes:** All mean ± standard deviations for mean age.

**Table 2** Preoperative and postoperative mean IOP (mmHg)

Time	Mean IOP change (mmHg) + DS (Range)						
	Control group	Range	Acetazolamide group	Range	Dorzolamide group	Range	P Value between groups and within groups
Preoperative	12.09 ± 3.19	15	12.08 ± 3.67	16	10.63 ± 2.87	11	0.035
Postoperative							
16 hours	16.80 ± 8.04	37	13.11 ± 6.08	24	17.80 ± 8.22	36	0.008
24 hours	11.66 ± 5.11	26	10.61 ± 4.26	22	11.74 ± 5.03	29	0.452
48 hours	10.90 ± 3.65	18	10.01 ± 2.34	13.5	9.75 ± 2.99	18	0.138

**Abbreviation:** IOP, intraocular pressure.

Acetazolamide 250 mg one tablet one hour preoperatively followed by half a tablet 125 mg every eight hours showed a statistically significant reduction in the IOP spike postoperatively at 16, 24, and 48 hours. A previous study reported the preoperative use of topical dorzolamide<sup>37</sup> and a dorzolamide–timolol combination.<sup>38</sup> These were effective in reducing IOP at six and 24 hours. Another study using acetazolamide 500 mg administered at one hour before

surgery showed significantly reduced IOP at four to six hours and 24 hours and fewer pressure spikes above 35 mmHg.<sup>39</sup> However, another study using the same dose one hour after surgery found no significant benefit.<sup>40</sup>

Carbonic anhydrase inhibitors have been used to treat glaucoma since 1954, when Becker<sup>41</sup> first demonstrated the clinical efficacy of acetazolamide. CAIs are sulfonamide derivatives that lower IOP by decreasing aqueous

**Table 3** Mean difference IOP change (mmHg) ± SE from preoperative to 16, 24, and 48 hours postoperatively

Dependent variable	(I) medicine	(J) medicine	Mean difference (I–J)	Std Error	Sig
Base IOP	Control groups	Acetazolamide groups	0.01	0.66	1
		Dorzolamide groups	1.46	0.63	0.073
	Acetazolamide groups	Control groups	–0.01	0.66	1
		Dorzolamide groups	1.44	0.66	0.093
	Dorzolamide groups	Control groups	–1.46	0.63	0.073
		Acetazolamide groups	–1.44	0.66	0.093
IOP 16 hours	Control groups	Acetazolamide groups	3.69	1.54	0.061
		Dorzolamide groups	–0.98	1.48	0.803
	Acetazolamide groups	Control groups	–3.69	1.54	0.061
		Dorzolamide groups	–4.67	1.54	0.011
	Dorzolamide groups	Control groups	0.98	1.48	0.803
		Acetazolamide groups	4.67	1.54	0.011
IOP 24 hours	Control groups	Acetazolamide groups	1.05	0.99	0.57
		Dorzolamide groups	–0.08	0.96	1
	Acetazolamide groups	Control groups	–1.05	0.99	0.57
		Dorzolamide groups	–1.13	0.98	0.519
	Dorzolamide groups	Control groups	0.08	0.95	1
		Acetazolamide groups	1.13	0.98	0.519
IOP 48 hours	Control groups	Acetazolamide groups	0.9	0.63	0.36
		Dorzolamide groups	1.15	0.6	0.162
	Acetazolamide groups	Control groups	–0.9	0.63	0.36
		Dorzolamide groups	0.25	0.62	0.92
	Dorzolamide groups	Control groups	–1.15	0.6	0.162
		Acetazolamide groups	–0.25	0.62	0.92

**Note:** The mean difference is significant at the 0.05 level.

**Abbreviations:** IOP, intraocular pressure; SE, standard error.

humor formation. These drugs inhibit carbonic anhydrase, which is one of the enzymes that regulate aqueous humor formation. Systemic administration of CAIs is extremely effective in reducing IOP in most patients but is accompanied by side effects that can range from mild and annoying to debilitating and life threatening, the latter necessitating discontinuation of these drugs. On rare occasions, CAIs may induce irreversible blood dyscrasias, which can be fatal. The substantial incidence of side effects and the rare occurrence of fatal complications have led to controversy regarding the usefulness of and indications for systemically administered CAIs in the chronic management of glaucoma.<sup>42</sup> CAIs reduce IOP by inhibiting aqueous humor formation. This has been demonstrated with the use of indirect measurement techniques<sup>43,44</sup> as well as direct fluorophotometric measurement techniques of aqueous humor flow rates.<sup>45–47</sup> Fluorophotometric studies have documented reductions in aqueous humor flow rates of 21% to 40% in normal human volunteers and in a few glaucoma patients after acute oral dosing with 250 to 750 mg acetazolamide.<sup>45–47</sup> McCannel and colleagues<sup>24</sup> found that acetazolamide reduced aqueous flow rates by 24% below the nocturnal flow rate in the eye of a sleeping patient. Timolol does not produce such reactions.

In conclusion, we found that acetazolamide effectively reduced the IOP spike, 16 hours and 24 to 48 hours after scleral tunnel cataract surgery with hard posterior chamber IOL implantation. The mean IOP significantly increased in placebo and dorzolamide groups, 16 hours after surgery. IOP monitoring in the early postoperative period is still necessary after scleral tunnel cataract surgery with viscoelastic substance. It may be possible therefore to select patients at greater risk who developed ocular hypertension after cataract surgery to receive prophylactic IOP-lowering treatment. This would minimize patient morbidity yielding significant health economic savings.

## Acknowledgments

I would like to thank my coauthors, Dr Motaher Al-Shaer, Dr Nabil Al-Matary, and Dr Mahfoud Bamashmous. Also many thanks are extended to Dr Yahia Raja and Dr Adnan Al-Adhal at the Department of Community Medicine and Department of Pharmacology, respectively, Sana'a University for their co-operation in evaluation of statistical analysis. I would like to thank all ophthalmic surgeons who did the work including the theatre attendants at the ophthalmic department, Sana'a University. Finally I wish to thank Dr Talal A. Haider, head of the ophthalmic department

of Sana'a University for his research advice. The authors report no conflicts of interest in this work.

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