

# Dorzolamide Hydrochloride %2 and Timolol Maleate %0.5 Fixed Combination in Lowering Intraocular Pressure after Phacoemulsification Cataract Surgery

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## Abstract

**Background and objectives:** To evaluate the role of dorzolamide –timolol fixed combination in lowering intraocular pressure (IOP) after cataract surgery. **Methods:** The study included 94 eyes of 89 patients who underwent cataract surgery and intraocular lens implantation. Patients planned for phacoemulsification were assigned to 1 of 2 groups. The treatment group received 1 drop of dorzolamide-timolol fixed combination immediately after surgery, and the control group received no treatment. The IOP was measured preoperatively and at 6 hours and 24 hours postoperatively. **Results:** The mean IOP change was lower in the treatment group than in the control group at 6 hours postoperatively. The difference between the mean IOP a value of the two groups at 6 hours postoperatively was found to be statistically significant. Twenty-four hours after the surgery, the mean IOP change was still higher in the control group when compared to the treatment group. **Conclusions:** The fixed combination dorzolamide-timolol can effectively lower IOP after phacoemulsification cataract surgery.

**Keywords:** Dorzolamide; Timolol; Cataract surgery.

## Introduction

Intraocular pressure (IOP) may increase in the postoperative period of cataract surgery. The incidence of postoperative IOP rise ranges between 15% and 60% within 24 hours<sup>1</sup>. The rises in IOP in the early postoperative period in healthy eyes after uncomplicated phacoemulsification cataract surgery have also previously been reported. Although most IOP elevations will return to normal within 24 hours postoperatively, there are some cases with extended IOP elevations more than 24 hour<sup>2</sup>. The exact mechanism that causes this IOP rise has not been fully understood. It may be induced by mechanical obstruction, inflammation or damage to the trabecular meshwork structures. The spikes in IOP may cause ocular pain, corneal edema and optic nerve damage<sup>2-3</sup>. Various drugs, including carbonic anhydrase inhibitors, beta blockers, and prostaglandins have been used to prevent or reduce elevation of IOP after cataract surgery. The dorzolamide-timolol fixed combination is comprised of the carbonic anhydrase inhibitor dorzolamide and the beta-blocker timolol and is recommended to be dosed twice daily. It is delivered as a suspension

with a pH of 7.2 and is preserved with 0.01% benzalkonium chloride. The main indication of this combination is IOP reduction in adult patients with glaucoma or ocular hypertension<sup>4</sup> A study which evaluated the efficacy of brinzolamide -timolol fixed combination in IOP after phacoemulsification cataract surgery using Viscoat and Provisc is by Geograpopoulos et al<sup>5</sup> who have reported that a single dose prevented a significant IOP increase during the first 24 hours postoperatively. We conducted a prospective study to assess the effect of the dorzolamide and timolol fixed combination on IOP after cataract surgery with phacoemulsification using sodium hyaluronate.

## Patients and methods

This prospective study included 94 eyes of 89 consecutive patients who underwent phacoemulsification cataract surgery with foldable intraocular lens implantation. All participants are given written informed consent prior to their participation. Eyes with past ocular surgery, ocular trauma, ocular hypertension and glaucoma were excluded.

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The baseline IOP was measured by Goldmann applanation tonometry 1d before surgery. The patients were randomly assigned to treatment and control groups. Treatment group included 49 eyes, control group included 45 eyes. There were 46 female and 48 male patients in the study group. The mean ages of the control group and treatment group were  $64.35 \pm 7.83$  years and  $65.04 \pm 9.60$  years, consecutively. All cataract surgeries were performed by the same surgeon (Dr Ahmed Ismaeel Alnuaimy). Topical phenylephrine and tropicamide eye drops were instilled for mydriasis 1 hour before surgery. After topical anesthesia with tetracaine eye drops, the surgery was initiated with a main incision at 12 o'clock in all eyes. Injection of sodium hyaluronate 1% which is a cohesive viscoelastic substance and only this type was used in the study, capsulorhexis, two side-port, hydrodissection and phacoemulsification followed. Capsular bag was expanded using again sodium hyaluronate and foldable intraocular lens was implanted into the bag in all eyes. The viscoelastic material was aspirated from the eye using bimanual irrigation/ aspiration tip. The incisions were hydrated finally. Rupture of posterior capsule or vitreous loss did not occur in any of the operated eyes. Immediately after surgery, the treatment group received a single drop of dorzolamide-timolol fixed combination in a strict sterile condition (opening the sterile sealed drop and aspiration of the drug into sterile syringes) the patients in control group did not receive any IOP lowering agents. All patients were treated with prednisolone and gatifloxacin eyedrops four times a day after surgery, and the dosages were tapered gradually. IOP was measured 6 hours and 24 hours after surgery in all patients by Goldman applanation tonometer. The IOP was measured by the same investigator during the study. Statistical analysis was done by SSPS statistical software (SPSS for windows 19.0, Inc., Chicago, USA). Group comparisons were made using paired t-tests for the same group, and independent t-test between different groups. Data were expressed as mean  $\pm$  standard deviation. Statistical significance was defined at a level of 5% ( $P < 0.05$ ).

## Results

Table 1 shows the demographic data of each study group.

**Table (1):** Demographic data in each study group.

Parameter	Control	Treatment
Eyes	45	49
Age	$64.35 \pm 7.83$	$65.04 \pm 9.60$
Male	27	21
Female	18	28

Table 2 shows the mean preoperative and postoperative IOPs in both groups.

**Table (2):** Mean IOP difference between study groups.

IOP(mmHg)	Control	Treatment	P
Preop.	$15.70 \pm 3.12$	$16.18 \pm 2.40$	0.400
Postop. 6hr	$26.21 \pm 10.72$	$16.00 \pm 2.39$	0.001
Postop. 24hr	$18.31 \pm 4.69$	$15.18 \pm 2.57$	0.001

Table 3 shows the comparison of IOP measurements postoperatively and preoperatively in each group.

**Table (3):** Mean IOP in each group (paired t-test).

IOP(mmHg)	Preop.	Postop. 6hr	P	Postop. 24hr	P
Control	15.70 ± 3.12	26.21 ± 10.72	<0.001	18.31 ± 4.69	0.001
Treatment	16.18 ± 2.40	16.00 ± 2.39	0.563	15.18 ± 2.57	0.01

In the treatment group, the mean IOP did not increase significantly at 6 hours after cataract surgery when compared with preoperative measurements ( $p = 0.563$ ), while the IOP decreased significantly after 24 hours when compared with preoperative measurements ( $p = 0.01$ ). In the control group, mean IOP increased significantly at 6 hours ( $p = 0.001$ ) and decreased but still significantly higher than the baseline levels at 24 hours postoperatively ( $p = 0.001$ ). There was no statistically significant difference when mean preoperative IOPs were compared between the two study groups ( $p = 0.400$ ). However, the mean IOP at 6 hours was found to be increased significantly in the control group ( $p = 0.001$ ). There were 6 cases of control group have 6hr postoperative IOP more than 40mmHg, two of them more than 50mmHg and treated by burbling the main incision (pressing the scleral side of the wound and releasing some amount of aqueous humor outside the eye) and they received IOP lowering treatment and excluded from the study. However, there was no rise of IOP in the treatment group more than 30mmHg after 6 hours postoperatively. No systemic or local side effects of dorzolamide-timolol fixed combination were observed during the study.

## Discussion

Cataract extraction is one of the most commonly performed and successful surgical procedures. Phacoemulsification and intraocular lens implantation is one of the most cost-effective, elective surgical interventions. Elevated IOP is the most frequent postoperative complication needing treatment following phacoemulsification. In order to minimize postoperative IOP rise, prophylaxis may

be adopted. Currently, there are no specific guidelines for IOP rise prophylaxis in uncomplicated cataract surgery. The causes of the elevated IOP are likely multifactorial. The exact mechanism of IOP elevation postoperatively is not known. It is attributed to many reasons, including occlusion of the trabecular meshwork by retention of viscoelastic and lenticular material, and inflammatory cells<sup>2</sup>. The timing of the first postoperative IOP check varied. 10.9% of surgeons reported the first IOP check was carried out on the same day, 29.7% on the first postoperative day, 20.8% by the first week, 26.9% at 2 weeks, and 9.5% beyond 2 weeks<sup>8</sup>. In the UK, 87% of surgeons who use IOP prophylaxis prefer oral Diamox over the topical agents<sup>8</sup>. Currently, there are no specific guidelines for IOP increase prophylaxis in uncomplicated cataract surgery, for this reason, we designed this study. The fixed-combination dorzolamide/timolol is safe and well tolerated for long-term treatment in patients with open-angle glaucoma or ocular hypertension patients<sup>15,19</sup>. As known timolol inhibits aqueous secretion and brinzolamide lowers aqueous production, and both mechanisms might have played a role in the reduction of IOP in the operated eyes. A significant portion of patients may experience an IOP greater than 28mmHg following phacoemulsification, but most IOP will return to normal by 24 hours postoperatively<sup>11</sup>. After uneventful phacoemulsification in eyes without glaucoma, however, IOP spikes may even reach 68mmHg. In most patients, postoperative increases in IOP are transient and benign<sup>12</sup>. In individuals without glaucoma, no visual field defects were evident once the IOP returned to normal. There are several drugs used to lower IOP after cataract surgery. The classes of drugs used to treat postoperative

increases in IOP include carbonic anhydrase inhibitors, alpha agonists, prostaglandin analogs, beta-blockers, and fixed combinations. Acetazolamide has been used for many years to treat IOP increases following cataract extraction and has proven moderately successful. This carbonic anhydrase inhibitor was more effective than topical apraclonidine, an alpha agonist, in a head-to-head trial<sup>13</sup>. Kemal Ornek et al found the brinzolamide and timolol combination is effective in controlling IOP spikes after phacoemulsification<sup>3</sup>. Another study showed that mean IOP in 24 hours following cataract extraction was greater than 21mmHg in the acetazolamide group and less than 21mmHg in the dorzolamide group<sup>14</sup>. Brinzolamide has been shown to be as effective as dorzolamide in controlling IOP postoperatively, but it is associated with less ocular discomfort following administration<sup>14</sup>. A study comparing acetazolamide and brinzolamide found that the drugs were equally effective at 4 hours to 6 hours after cataract surgery but that only brinzolamide produced a statistically significant decrease in IOP at 24 hours<sup>14</sup>. Rainer et al<sup>15</sup> compared dorzolamide and latanoprost, a prostaglandin analog. Both drugs produced a clinically significant reduction in IOP 6 hours after cataract surgery, but only dorzolamide was effective at 24 hours. A comparison of travoprost and brinzolamide showed that both produced a clinically significant decrease in IOP 6h and 24 hours postoperatively. Neither, however, was always able to prevent a spike greater than 30mmHg<sup>16</sup>. Rainer et al<sup>18</sup> compared a fixed dorzolamide-timolol combination with latanoprost. The fixed combination reduced postoperative IOP more effectively, and it prevented any increase in IOP to greater than 30mmHg<sup>18</sup>. Another study comparing a dorzolamide-timolol combination to placebo found the fixed combination to produce a clinically significant reduction in postoperative IOP. The agent, however, did not completely prevent IOP spikes greater than 30mmHg<sup>7</sup>. In a recent study, Georgakopoulos et al<sup>10</sup> have reported that a single dose of brinzolamide-timolol fixed combination prevented a significant IOP increase during the first 24 hours postoperatively.

This study is to evaluate the efficacy of dorzolamide-timolol fixed combination in reducing the transient IOP increase after phacoemulsification surgery. The results showed that a single postoperative administration of fixed dorzolamide-timolol combination was significantly effective in reducing IOP after cataract surgery using sodium hyaluronate. Six hours and 24 hours after surgery, the mean IOP was lower in the dorzolamide-timolol combination group than in the control group. The increase in IOP was significant at 6 hours and 24 hours in the control group. There was also a significant difference in the amount of IOP increase between the two groups. In the treatment group of current, no eye had an IOP rise over 30mmHg and in control group 6 eyes had IOP over 40mmHg at 6h. These eyes received additional anti-glaucoma medication as the IOP exceeded safety levels. Rainer et al<sup>15</sup> have found that after cataract surgery using hydroxypropyl methylcellulose, a single measurement at 2 hours postoperatively could detect two thirds of IOP spikes.

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## Conclusions

In conclusion, our study showed that postoperative administration of dorzolamide-timolol fixed combination was effective in reducing IOP after phacoemulsification cataract surgery. Ophthalmologists must be aware of the potential for postoperative increases in IOP spikes following uncomplicated phacoemulsification, know the risk factors for this complication, and treat their patients with a variety of treatment options.

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