Effect of 1% brinzolamide and 0.5% timolol fixed combination on intraocular pressure after cataract surgery with phacoemulsification

Kemal Örnek, Nesrin Büyüktortop, Nurgül Örnek, Reş汗an Ogurel, İnci Elif Erbahçeci, Zafer Onaran

Department of Ophthalmology, School of Medicine, Kırıkkale University, Kırıkkale 71100, Turkey

Corresponding to: Kemal Örnek. 1465. sokak, 16/31, Çukurambar, Çankaya, Ankara 06510, Turkey. kemalornek@hotmail.com

Received: 2013-01-04 Accepted: 2013-08-01

Abstract

- AIM: To evaluate the effect of brinzolamide–timolol fixed combination on intraocular pressure (IOP) after cataract surgery.
- METHODS: The study included 92 eyes of 87 patients who underwent cataract surgery and intraocular lens implantation. Patients scheduled for phacoemulsification were assigned to 1 of 2 groups. The treatment group received 1 drop of brinzolamide–timolol fixed combination immediately after surgery, and the control group received no treatment. The IOP was measured preoperatively and at 2h and 24h postoperatively.
- RESULTS: The mean IOP change was lower in the treatment group than in the control group at 2h postoperatively. The difference between the mean IOP values of the two groups at 2h 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.
- CONCLUSION: The fixed combination brinzolamide – timolol can effectively reduce IOP after cataract surgery.
- KEYWORDS: brinzolamide; timolol; cataract surgery

DOI:10.3980/j.issn.2222–3959.2013.06.19

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 24h [1]. The exact mechanism underlying this IOP rise has not been elucidated. It may be induced by mechanical obstruction, inflammation or damage to the angle structures. It may cause ocular pain, corneal edema and optic nerve damage [2,3]. Various drugs, including carbonic anhydrase inhibitors, beta blockers, prostaglandins have been used to prevent or reduce elevation of IOP after cataract surgery [4-8,10-24].

The brinzolamide-timolol fixed combination is comprised of the carbonic anhydrase inhibitor brinzolamide 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 [9]. Only study by Georgakopoulos et al. [10] evaluated the efficacy of brinzolamide-timolol fixed combination in IOP after phacoemulsification cataract surgery using Viscoat and Provisc and have reported that a single dose prevented a significant IOP increase during the first 24h postoperatively.

We conducted a prospective study to assess the effect of the brinzolamide and timolol fixed combination on IOP after cataract surgery with phacoemulsification using hydroxypropyl methylcellulose.
All cataract surgeries were performed by the same surgeon (Ornek) who was masked to treatment assignment. Topical phenylephrine, tropicamide and cyclopentolate eyedrops were instilled for mydriasis 1h before surgery. After retrobulbar anesthesia, the surgery was initiated with two side-port and a main temporal incision in all eyes. Injection of hydroxypropyl methylcellulose, capsulorhexis, hydrodissection and phacoemulsification followed. Capsular bag was expanded using again hydroxypropyl methylcellulose 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 brinzolamide-timolol fixed combination. The patients in control group did not receive any IOP lowering agents. All patients were treated with dexamethasone and tobramycin eyedrops four times a day after surgery, and the dosages were tapered gradually. IOP was measured 2h and 24h after surgery in all groups by Goldmann applanation tonometry. The IOP was measured by the same investigator during the study who was masked to the treatment group.

Statistical Analysis  Statistical analysis was done by SPSS statistical software (SPSS for windows 10.0, Inc., Chicago, USA). Group comparisons were made using paired t-tests. Data were expressed as mean±standard deviation ( ividuals 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, fixed combinations etc.

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 5. Another study showed that mean IOP in 24h following cataract extraction was greater than 21mmHg in the acetazolamide group and less than 21mmHg in the dorzolamide group4. Brinzolamide has been shown to
be as effective as dorzolamide in controlling IOP postoperatively, but it is associated with less ocular discomfort following administration [14]. A study comparing acetazolamide and brinzolamide found that the drugs were equally effective at 4h to 6h after cataract surgery but that only brinzolamide produced a statistically significant decrease in IOP at 24h[16].

Rainer et al [15] compared dorzolamide and latanoprost, a prostaglandin analog. Both drugs produced a clinically significant reduction in IOP 6h after cataract surgery, but only dorzolamide was effective at 24h. A comparison of travoprost and brinzolamide showed that both produced a clinically significant decrease in IOP 6h and 24h postoperatively. Neither, however, was always able to prevent a spike greater than 30mmHg[16].

Arici et al[16] have shown that both latanoprost and travoprost could prevent postoperative IOP elevation safely. In another study, timolol but not latanoprost was effective in reducing postoperative IOP. In fact, patients receiving one drop of timolol at the end of surgery had a mean decrease in IOP of 4.77mmHg and 2.99mmHg at 4h and 24h, respectively[17].

Rainer et al [18] 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 [18]. 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 [7]. In a recent study, Georgakopoulos et al [18] have reported that a single dose of brinzolamide-timolol fixed combination prevented a significant IOP increase during the first 24h postoperatively.

This study is the second to to evaluate the efficacy of brinzolamide-timolol fixed combination in reducing the transient IOP increase after phacoemulsification surgery. The results showed that a single postoperative administration of fixed brinzolamide-timolol combination was significantly effective in reducing IOP after cataract surgery using hydroxypropyl methylcellulose. Two hours and 24h after surgery, the mean IOP was lower in the brinzolamide-timolol combination group than in the control group. The increase was significant at 2h in the control group. There was also a significant difference in the amount of IOP increase between the two groups. In treatment group, 8 eyes had an IOP increase of 5mmHg or more, however in controls 23 eyes had the same amount of IOP increase postoperatively. In the treatment group, 3 eyes had an IOP rise over 30mmHg and in control group 9 eyes had IOP over 30mmHg at 2h. These eyes received additional anti-glaucoma medication as the IOP exceeded safety levels.

It has been accepted that timolol does not lower IOP at night, but it seems that only PGAs may accomplish that anyway. There is a lack of consensus regarding the efficacy of the IOP-lowering drugs at night. Some studies have reported that timolol lowers IOP at night when it is used alone or in a fixed combination with a carbonic anhydrase inhibitor or a prostaglandin analogue [19-21]. Other studies did not find any IOP lowering effects with a β-blocker during the night [22-23].

One study demonstrated that brinzolamide/timolol fixed combination achieved a better mean 24-h IOP control owing to the greater efficacy in late afternoon and during the night [24]. Rainer et al [25] have found that after cataract surgery using hydroxypropylmethylcellulose, a single measurement at 2h postoperatively could detect two thirds of IOP spikes. In our study, although 16% of IOP spikes occurred at 2h when compared to control eyes, brinzolamide-timolol fixed combination reduced the elevated IOP in these eyes at 24h. 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.

In conclusion, our study showed that postoperative administration of brinzolamide-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.

REFERENCES

2003;29(9):1748–1752
9 Rossi GC, Tinelli G, Pasinetti GM, Fusetti M, Pallavicini C, Stringa M, Vecchi S, Stringa F, Bianchi PE. Signs and symptoms of ocular surface status in glaucoma patients switched from timolol 0.5% to brinzolamide 1% /timolol 0.5% fixed combination: a 6-month efficacy and tolerability, multicenter, open-label prospective study. Expert Opin Pharmacother 2011;12(5):685–690