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A topical or oral carbonic anhydrase inhibitor to control ocular hypertension after cataract surgery

Ö. E. ABBASOĞLU, O. TEKELI, A. ÇELIKDOĞAN, E. GÜRSEL

Ankara Numune Hospital 2, Eye Clinic, Ankara - Turkey

PURPOSE. *To compare the effects of oral acetozolamide and topical 2% dorzolamide to prevent ocular hypertension after cataract surgery.*
METHODS. *This prospective, randomized study comprised 62 consecutive patients who had extracapsular cataract extraction and posterior chamber intraocular lens implantation. Patients received either oral acetozolamide (Diazomide®) 250 mg three times daily or topical dorzolamide 2% (Trusopt®) three times daily, for three days. Intraocular pressures (IOP) were measured by Goldmann applanation tonometry preoperatively and 16, 40, 64 hours postoperatively.*
RESULTS. *IOP in the dorzolamide group peaked at 16 hours and had returned to preoperative values by 40 hours. In the acetozolamide group mean IOP was significantly higher than preoperative values at 16, 40 and 64 hours ($p<0.05$). At all three postoperative measurement times, mean IOP was significantly higher in the acetozolamide group ($p<0.05$).*
CONCLUSIONS. *Topical dorzolamide 2% offers better IOP control than oral acetozolamide to prevent ocular hypertension after cataract surgery. (Eur J Ophthalmol 2000; 10: 27-31)*

KEY WORDS: *Intraocular pressure, Dorzolamide, Acetozolamide, Cataract surgery*

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INTRODUCTION

Transient ocular hypertension after cataract surgery can be due to surgical trauma to the trabecular meshwork, inflammation, residual viscoelastic material, preexisting poor outflow or tight wound closure (1). It has been reported that 1.6-3.5 % of patients undergoing cataract surgery with posterior chamber intraocular lens (IOL) implantation develop glaucoma (2, 3).

Viscoelastics can cause ocular hypertension by obstructing outflow with their large molecules. Therefore, the general recommendation is to aspirate the viscoelastic agent from the anterior chamber at the end of surgery (4, 5).

Oral acetozolamide, topical beta blockers, aproclonidine, topical and intracameral miotics have all been tried to prevent postoperative ocular hypertension (6-10). We report a prospective, randomized study comparing the effects of oral acetozolamide with topical 2% dorzolamide to prevent IOP rising after cataract surgery.

PATIENTS AND METHODS

This prospective study comprised 62 consecutive patients who had extracapsular cataract extraction (ECCE) and posterior chamber IOL implantation between September 1997 and May 1998. Thirty-seven patients (59.7%) were male and 25 (40.3%) female. Their mean ages were 64.9±7.9 and 65.5 ± 8.6 years for those given acetozolamide and dorzolamide respectively.

All patients had senile cataracts. Only one eye from

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each patient was included in the study. Patients with pseudoexfoliation, history of uveitis, glaucoma, trauma and those who had complicated surgery were excluded. Patients who used systemic medications such as steroids, calcium channel blockers, etc. that might affect IOP were also excluded. All patients had IOP below 20 mm Hg before surgery.

Equal numbers of patients were randomly assigned to two groups. Patients in group I received oral acetozolamide (Diazomide®) 250 mg three times daily starting 15 minutes after surgery, for three days. Patients in group II received topical dorzolamide 2% three times daily, starting immediately after surgery, for three days. Each patient also received topical dexamethasone (Dexasine®) and gentamicin (Gentagut®) three times daily in the operated eye. We had no untreated control group because we observe significant IOP rises after surgery and routinely use prophylactic antiglaucoma medications in the early postoperative period.

The surgical technique was standard in all cases. Osmotic agents were not used preoperatively. All patients had retrobulbar anesthesia using a 50/50 mixture of 0.75% bupivacaine hydrochloride (Marcaine®) and 2% lidocaine with epinephrine. A fornix-based conjunctival flap was made. The corneoscleral beveled incison was approximately 8 mm long. Sodium hyaluronate (Healon®) was given into anterior chamber and can-opener capsulotomy was done. After hydrodissection and lens delivery through the incision, cortical aspiration was done with a Simcoe irrigation aspiration cannula. Healon was used to form the anterior chamber and a posterior chamber IOL (Ophthalmed 6.5 mm optic diameter, biconvex optic) was implanted in the sulcus or capsular bag. The healon was meticulously aspirated with the Simcoe irrigation aspiration cannula. All patients received intracameral acetylcholine chloride. The incision was closed with 10/0 nylon interrupted sutures. At the end of surgery patients received subconjunctival 2 mg/0.5 ml dexamethazone and gentamicin. All patients had an uneventful recovery.

The first postoperative IOP measurement was done at 16 hours for practical reasons. Subsequent measurements were taken 40 and 64 hours postoperatively using a Goldmann tonometer. Patients were questioned for any untoward effects like paresthesia, tingling, malaise, abdominal pain, tinnitus,stinging on instillation and metallic taste.

Data were analyzed with Student's t-test and the chi-square test. P values <0.05 were considered significant.

RESULTS

There were no significant differences in age, sex and mean preoperative IOP in groups I and II ($p>0.05$). Preoperative and postoperative mean IOP at 16, 40 and 64 hours are summarized in Table I. In the acetozolamide group, mean IOP at 16, 40 and 64 hours was significantly higher than preoperative mean IOP, with a significant difference between mean IOP at 16-40 hours and 40-64 hours ($p<0.05$).

In the dorzolamide group, mean IOP at postoperative 16 hours was significantly higher than preoperative mean IOP ($p<0.05$) but significantly lower than that of the acetozolamide group at 16 hours ($p<0.05$). Mean IOP at 40 and 64 hours did not show any real

TABLE I - PREOPERATIVE AND 16, 40, AND 64 HOUR POSTOPERATIVE MEAN IOP OF PATIENTS GIVEN ACETOZOLAMIDE OR DORZOLAMIDE

	Group I Acetozolamide Mean ± SD IOP	**Group II Dorzolamide 2% Mean ± SD IOP**	**p value**
Preoperative	14.12 ± 2.17	13.61 ± 2.55	>0.05
Postoperative			
16 hours	19.12 ± 3.64	17.14 ± 2.54	<0.05
40 hours	16.87 ± 3.28	14.38 ± 2.60	<0.01
64 hours	15.87 ± 2.57	14.16 ± 2.63	<0.05

SD: Standard deviation

difference from preoperative mean IOP or from each other. Thus mean IOP in the dorzolamide group increased less than in the acetozolamide group, returning to preoperative values by postoperative 40 hours and still stable at 64 hours (Fig. 1).

At 16 hours the mean increase in IOP in the acetozolamide and dorzolamide groups, compared with the preoperative means, were respectively 5.00 ± 4.04 and 3.54 ± 3.65 mm Hg ($p<0.05$). Mean decreases in IOP at 40 hours, compared with mean IOP at 16 hours, were respectively 2.25 ± 3.68 and 2.77 ± 2.56 mm Hg ($p<0.05$). Mean differences in IOP between postoperative 40 and 64 hours showed mean decreases of 1.00 ± 2.16 and 0.22 ± 2.12 mm Hg ($p<0.05$) respectively.

Seven patients in the acetozolamide group (22.6%) and two in the dorzolamide group (6.5%) had IOP higher than 20 mm Hg at 16 h (NS). However at 40 h, six patients (19.4%) in the acetozolamide group and one (3.2%) in the dorzolamide group had IOP higher than 20 mm Hg; this was significant ($p<0.05$). None of the patients had postoperative IOP higher than 30 mm Hg.

In the acetozolamide group six patients (19.4%) reported paresthesia, four (12.9%) malaise, one (3.2%) tinnitus and one (3.2%) abdominal discomfort. In the dorzolamide group six patients (19.4%) had stinging on instillation of the drops and four (12.9%) had a bitter taste. None of the patients in the dorzolamide group had systemic adverse effects.

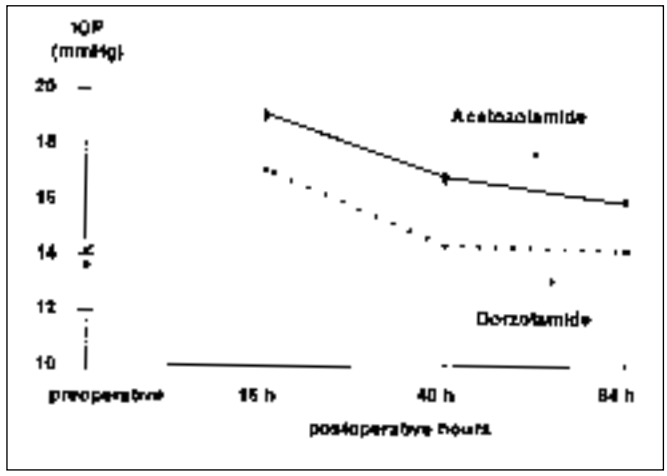

Fig. 1 - *Mean IOP in the acetozolamide and dorzolamide groups in relation to time. The fine dotted lines between preoperative IOP values and 16 hour measurements indicate the pattern of IOP increase. IOP sometimes spiked in the very early postoperative hours.*

DISCUSSION

Viscoelastic-induced ocular hypertension after cataract surgery is amply documented (4-8) and particularly during the first 24 hours IOP can reach high levels (4, 5). In our study all patients had significant IOP rises 16 hours after surgery, the increase being significantly greater in the acetozolamide than the dorzolamide group.

After the initial rise in IOP at 16 h, both drugs significantly lowered mean IOP. In the dorzolamide group IOP returned to the preoperative values by 40 hours whereas in the acetozolamide group IOP was still significantly higher than preoperative values at postoperative 64 hours. Thus dorzolamide caused a significantly better decrease in mean IOP.

More patients had postoperative IOP higher than 20 mm Hg in the acetozolamide group at 16 and 40 h. At 40 h the difference was statistically significant. This also shows the better IOP control by dorzolamide. None of the patients had postoperative IOP higher than 30 mm Hg, possibly because of intracameral acetylcholine administration at the end of the surgery.

Oral acetozolamide has been tested for the prevention of postoperative ocular hypertension (6-8, 11). Lewen et al reported that a dose of 250 mg qid was effective in preventing the IOP rise after cataract surgery (11). Fry compared the effects of seven different antiglaucoma medications in controlling viscoelastic-induced IOP after ECCE (6). A single oral dose of 500 mg acetozolamide postoperatively gave a 15% reduction in IOP. This effect was comparable to the effects of timoptic, pilopine gel and betagan and was more than that of betoptic and iopidine. In that study mean IOP in the acetozolamide group returned to preoperative levels in 2-7 days.

Although very effective in controlling IOP rises, oral acetozolamide and beta-blockers have serious potential side effects. Acetozolamide can cause fatal aplastic anemia, nephrolithiasis and sulpha allergy (12). Beta-blockers, especially non-selective ones, can aggravate restrictive and obstructive pulmonary diseases, and can cause potentially fatal cardiac problems (13).

Dorzolamide has opened new horizons for IOP control as it is as effective as oral acetozolamide with fewer side effects (14). A one-year comparative study

showed that the ocular hypotensive efficacy of dorzolamide 2% three times daily was similar to that of betaxolol 0.5% twice daily, and slightly inferior to that of timolol 0.5% twice daily (15). Dorzolamide 2% used topically three times daily caused a 18.0 - 22.9% decrease in IOP in patients with open angle glaucoma and ocular hypertension (15, 16). When used to control the IOP rise after Nd:YAG posterior capsulotomy, a preoperative single drop of dorzolamide 2% achieved a mean IOP of 16.7 mm Hg at 24 hours. It had comparable high efficacy to oral acetozolamide (17).

A study by Zohdy et al compared the effects of a postoperative single oral dose of 250 mg acetozolamide with one drop dorzolamide 2% after uncomplicated phacoemulsification surgery (18). Dorzolamide was more effective than acetozolamide 4 h after surgery but equally effective at 24 h.

In our study dorzolamide controlled the acute IOP rise after surgery and lowered IOP from its peak to preoperative values sooner than oral acetozolamide. The success of dorzolamide is probably due to its pharmacological properties, like the good balance between water and lipid solubility, high activity against carbonic anhydrase in 2% aqueous solution and a corneal depot effect (19). Topical dorzolamide causes none of the systemic side effects attributable to oral carbonic anhydrase inhibitors. So it is a safe, effective medication to control the postoperative IOP rise without systemic adverse reactions.

Reprint requests to:
Özlem Evren Abbasoğlu, MD
Birlik Mah. 9. Cad.
Altinçay Sitesi C Blok No17
Çankaya Ankara, 06610 Turkey
e-mail: oevren-abbasoglu@usa.net

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