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Short-term effect of topical brinzolamide on human central corneal thickness

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PURPOSE. *To investigate the effect of short-term brinzolamide application on human central corneal thickness (CCT).*

METHODS. *Seventeen eyes of 16 patients who underwent neodymium:YAG laser posterior capsulotomy were included in the study group. Twenty-two subjects served as controls. Brinzolamide twice daily and fluorometholone four times daily were initiated after the procedure. Corneal thickness was evaluated with an ultrasound pachymetry from the central region. CCT measurements were performed before the procedure, at first day, and at the end of first week.*

RESULTS. *The mean baseline CCT value was 535.1±37.8 μm. In comparison to the control group (546.4±22.2 μm), there was no statistically significant difference (p=0.248). After brinzolamide instillation, the mean CCT values at first day and at first week was measured as 545.1±40.1 μm and 538.8±39.4 μm, respectively. The difference at first day was statistically significant when compared to the baseline values (p=0.00017). When compared to the control group, no statistically significant difference was observed for the mean CCT values of the first day and first week (p=0.906 and p=0.484, respectively). In the fellow eyes, mean CCT values increased following the dorzolamide instillation (529.3±42.6 μm, 534±41.7 μm, and 533±41.9 μm, respectively). No statistically significant difference was observed between the control group and fellow eye group when compared (p=0.162, p=0.247, p=0.270, respectively).*

CONCLUSIONS. *Brinzolamide may cause a short-term increase in the human CCT, particularly on the first day. (Eur J Ophthalmol 2008; 18: 338-40)*

KEY WORDS. *Brinzolamide, Central corneal thickness*

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INTRODUCTION

Brinzolamide is a highly specific carbonic anhydrase inhibitor which lowers intraocular pressure by decreasing aqueous humor secretion. Formulated as a 1% ophthalmic suspension (Azopt; Alcon Laboratories, Fort Worth, TX) and administered twice or three times daily, brinzolamide is indicated for the topical management of primary open-angle glaucoma and ocular hypertension as either monotherapy or adjunctive therapy (1). Brinzolamide has also been shown to be effective in preventing intraocular pressure rise after neodymium:YAG (Nd:YAG) laser posterior capsulotomy when compared to apraclonidine in a recent study (2).

In clinical trials, brinzolamide was well tolerated causing only nonserious adverse effects that were generally local, transient, and mild to moderate in severity. The incidence of the most common adverse events associated with the use of brinzolamide was either similar to (blurred vision and abnormal taste) or significantly lower than (ocular discomfort) with dorzolamide (3).

Up to now, the studies on the effect of topical carbonic anhydrase inhibitors on human corneal thickness were all conducted using dorzolamide (4-7). To our knowledge, there are little clinical data concerning the effect of brinzolamide on human cornea.

The aim of our study was to investigate the effect of short-term brinzolamide application on central corneal

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thickness (CCT) of patients who received Nd:YAG laser posterior capsulotomy for posterior capsular opacification.

METHODS

Two sex- and age-matched groups were constituted for this study. There were 6 (38%) men and 10 (62%) women in the brinzolamide group with a mean age of 61.5±23.9 years. Control group included 22 subjects (10 men and 12 women) with a mean age of 58.0±19.4 years. Seventeen eyes of 16 patients who received neodymium:YAG laser posterior capsulotomy were included in the study group. Informed consent was provided from each participant after giving detailed information. All patients underwent a complete ophthalmologic examination including refraction, external eye examination, slit-lamp examination, and fundus evaluation before the procedure. People with a history of corneal disease, ocular trauma, and taking other topical medications were excluded. All had history of the same ocular surgery (phacoemulsification with posterior intraocular lens implantation).

Posterior capsulotomy was performed using neodymium:YAG laser (Lpulsa SYL9000, LightMed, Taiwan) in all patients. Brinzolamide (Azopt) twice daily and fluorometholone (FML; Allergan) four times daily were initiated for each patient after neodymium:YAG laser posterior capsulotomy to control intraocular pressure elevation and inflammation. The drug regimen was used for 1 week in all patients. CCT measurements were all performed in the morning (9:00 AM) before the procedure, at first day, and at the end of first week.

Corneal thickness was evaluated with ultrasound pachymetry (Pacline, Optikon, Italy) from the central region after instillation of topical proparacaine hydrochloride just before the ophthalmologic examination at each time by the same examiner. The average of four consecutive readings were taken as the final score.

The results were expressed as mean ± SD and were analyzed statistically using paired Student *t* tests. p Values less than 0.05 were considered statistically significant.

RESULTS

Intraocular pressure readings were in normal limits before the capsulotomy and did not differ significantly at control visits. No significant intraocular inflammation was observed after the procedure in the patients' eyes.

The mean CCT value before the capsulotomy and instillation of brinzolamide was found to be 535.1±37.8 µm. In comparison to the control group (mean 546.4±22.2 µm), there was no statistically significant difference (p=0.248). After initiating brinzolamide, the mean CCT values at first day and at first week were measured as 545.1±40.1 µm and 538.8±39.4 µm, respectively. The difference at first day was statistically significant when compared to the baseline values (p=0.00017). Although there was a slight thickening of the cornea at first week, the difference was found to be insignificant (p=0.08742). When compared to the control group, no statistically significant difference was observed for the mean CCT values of the first day and first week (p=0.906 and p=0.484, respectively).

In the dorzolamide fellow eyes, mean CCT values increased following the dorzolamide instillation (529.3±42.6 µm, 534±41.7 µm, and 533±41.9 µm, respectively) and nearly returned to the baseline levels by the end of the first week; the differences were statistically significant between the baseline values and the first day and between the baseline values and the first week values (p=0.000177 and p=0.000562, respectively). No statistically significant difference was observed between the control group and fellow eye group when compared (p=0.162, p=0.247, p=0.270, respectively). Table I lists the CCT values for the study group.

DISCUSSION

As the endothelial carbonic anhydrase has a role in the mechanism of fluid transportation, the use of carbonic anhydrase inhibitors like dorzolamide and brinzolamide may induce changes in the human cornea (4-9). Wilkerson et al (7) reported that corneal thickness increased in a group using dorzolamide; however, Lass et al did not find any differences in corneal thickness in patients using dorzo-

TABLE I - CENTRAL CORNEAL THICKNESS (CCT) VALUES OF SUBJECT EYE AND FELLOW EYE

	Mean CCT Baseline	Mean CCT at first day	Mean CCT at first week
Brinzolamide eye	535.1±37.8	545.1±40.1	538.8±39.4
Fellow eye	529.3±42.6	534±41.7	533±41.9

lamide (6). In an animal study, dorzolamide was found to have no significant effect on the CCT (4).

To date, the short-term effect of brinzolamide on human CCT has not been reported. Wang et al found no significant changes after 6 weeks of brinzolamide treatment in a group of patients with open angle glaucoma (1). In our study, mean CCT values approached the baseline values by the end of the first week in brinzolamide eyes; therefore after 6 weeks it is possible not to find a significant change in corneal thickening. As with potent carbonic anhydrase inhibitors like dorzolamide, we hoped to see a similar effect with the brinzolamide in this study. Although the results of the previous studies conducted using dorzolamide had some discrepancies, our results revealed a significant increase in CCT following a short-term application (4, 5).

In this study, we found a significant thickening of central cornea especially on the first day which continued during the following week. The thickening decreased gradually in the following days and there was still thicker cornea by the end of the first week when the medication was stopped. A physiologic adaptation or local counter regulatory mechanisms may be an explanation for the decrease in the CCT during the following days. Although the difference between the controls and the brinzolamide group was not statistically significant, a short term thickening effect of brinzolamide on human cornea was observed, as also seen in the fellow eyes. Absorption of brinzolamide through the conjunctiva or the mucosa of the nasopharynx may have resulted in a slight thickening of the central cornea in the fellow eye.

Brinzolamide is a new topical carbonic anhydrase inhibitor for intraocular pressure control. It has high inhibitory activity against human carbonic anhydrase II, which is the key isoenzyme regulating aqueous humor production. These results indicate that like other antiglaucoma drugs, brinzolamide may interfere with the physiologic function of corneal endothelial cells and may cause a transient increase in the CCT (8, 9).

In conclusion, our study revealed a short-term increase in the human CCT following the use of brinzolamide. The increase was largest on the first day and throughout the following week it approximated the baseline values. These findings may help to evaluate the intraocular pressure lowering effect of brinzolamide in glaucoma patients or may be useful for patients with corneal endothelial dysfunctions before initiating the drug. Although our results were statistically significant, the changes on the central corneal pachymetry may not be clinically relevant. Further studies are needed to investigate the short-term and long-term effects of this new drug on human cornea.

Proprietary interest: None.

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