Brimonidine-Timolol Versus Dorzolamide-Timolol for Treatment of Intraocular Pressure Spikes After Phacoemulsification

Fakoemülsifikasyon Sonrası Göz İçi Basıncı Artışı Tedavisinde Brimonidin-Timolol ile Dorzolamide-Timolol'ün Karşılaştırılması

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ABSTARCT

Purpose: To compare the efficacies of fixed combination dorzolamide-timolol (FCDT) and fixed combination brimonidine-timolol (FCBT) for preventing intraocular pressure (IOP) spikes after phacoemulsification surgery.

Materials and Methods: One hundred and fifty eyes of 150 patients undergoing phacoemulsification surgery were enrolled in this study. Patients were randomly divided preoperatively into three groups according to the drug that instilled immediately after surgery; FCDT group that receiving one drop of FCDT, FCBT group that receiving one drop of FCBT and control group that receiving one drop of artificial tear. IOP was recorded immediately before surgery (baseline), at the 6th hour, 24th hour and 7th day postoperatively.

Results: Mean IOP levels were significantly lower in the treatment groups than in the control group at the 6th and 24th hours (both $p<0.001$) after surgery whereas there was no significant difference between the treatment groups during the follow-up period.

Conclusion: Our study has demonstrated that both FCDT and FCBT, each one drop administered immediately after procedure, were effective and both had similar efficacy for preventing IOP elevation after phacoemulsification surgery.

Key Words: Dorzolamide-timolol, brimonidine-timolol, intraocular pressure elevation, phacoemulsification.

ÖZ

Amaç: Fakoemülsifikasyon cerrahisi sonrası göz içi basıncı (GİB) yükselmesinin önlenmesinde dorzolamide-timolol sabit kombinasyonu (DTSK) ile brimonidine-timolol sabit kombinasyonu (BTSK)'nun etkinliklerinin karşılaştırılması.

Gereç ve Yöntem: Fakoemülsifikasyon cerrahisine giden 150 hastanın 150 gözü bu çalışmaya dahil edildi. Hastalar cerrahiden hemen sonra damlatılan damlalara göre rastgele üç gruba ayrıldı; DTSK grubuna 1 damla DTSK, BTSK grubuna 1 damla BTSK ve kontrol grubuna 1 damla suni gözyaşı damlatıldı. GİB her hasta için ameliyattan hemen önce ve ameliyat sonrası 6. saat, 24. saat ve 7. günlerde ölçüldü.

Bulgular: Ortalama GİB değerleri 6. ve 24. saatlerde DTSK ve BTSK gruplarında kontrol grubuna göre anlamlı derecede düşüktü ($p<0.001$). Ancak her iki tedavi grubunda takip süresi boyunca anlamlı bir fark yoktu.

Sonuç: Bu çalışma, işlem sonrası damlatılan bir damla DTSK veya BTSK'nın her ikisinin de fakoemulsifiakasyon cerrahisi sonrası GİB artışının önlenmesinde etkin olduğu ve benzer etkiye sahip olduklarını gösterdi.

Anahtar Kelimeler: Dorzolamide-timolol, brimonidine-timolol, göziçi basıncı yükselmesi, fakoemülsifikasyon.

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INTRODUCTION

Intraocular pressure (IOP) may rise significantly in the first 24 hours after cataract surgery. Studies have shown that the incidence of this IOP elevation varies from 15% to 60%.[1-3] Although in most cases this high pressure level is transient, it may cause ocular pain, corneal edema and vision-threatening complications (i.e. retinal artery occlusion, ischemic optic neuropathy and damage of neural tissue) especially in patients with pre-existing glaucoma or vascular insufficiency.[4-6]

In addition, current surgery is often performed on an outpatient basis and patient is discharged within few hours. Therefore, the first 24 hours period is of great importance for patients undergoing cataract surgery.[2]

Fixed combination dorzolamide-timolol (FCDT) has been approved by the US Food and Drug Administration (FDA) since 1998 and is widely used in patients with glaucoma.[7,8] Fixed combination brimonidine-timolol (FCBT) is another combination drug that is currently available for glaucoma treatment. Previous studies have compared the effectiveness of these fixed combinations for treatment of primary open angle glaucoma (POAG), pseudoexfoliative glaucoma (PXG) and ocular hypertension.[9-12]

However, to our best notice, there is no study comparing the effectiveness of aforementioned fixed combinations to prevent IOP elevation following phacoemulsification surgery. Therefore, the aim of our study was to compare the efficacies of FCDT and FCBT for preventing IOP spikes after phacoemulsification surgery.

MATERIALS AND METHODS

One hundred and fifty eyes of 150 patients undergoing phacoemulsification surgery and foldable intraocular lens implantation were enrolled in this prospective study. Patients were randomly divided preoperatively into three groups (each group including 50 eyes of 50 patients) according to the drug that instilled immediately after surgery as FCDT group (receiving one drop of FCDT (Cosopt, Merck and Co, Inc., Whitehouse Station, NJ, USA)], FCBT group [receiving one drop of FCBT (Combigan, Allergan, Inc., Irvine, CA, USA) and control group (receiving one drop of artificial tear). All patients were informed about the study procedure and they consented to participate. This study followed the Tenets of the Declaration of Helsinki and was approved by the Local Ethics Committee.

Exclusion criteria included a history of glaucoma or ocular surgery, corneal scar, pseudoexfoliation syndrome, pigment dispersion syndrome, ocular hypertension (IOP greater than 21 mmHg before the surgery), use of topical or systemic IOP-lowering medications, vitreous loss during surgery, known hypersensitivity to study medications or their components, cardiovascular diseases, and asthma.

IOP was recorded with Goldmann applanation tonometer immediately before surgery (baseline), at the 6th hour, 24th hour and 7th day postoperatively. Measurements were performed by the same ophthalmologist blinded to the groups and the average of the 2 measurements was used for analyses. An IOP higher than 30 mmHg or an IOP change of greater than 20 mmHg from baseline was an indication for exclusion from the study.

All patients were operated under sub-Tenon's anesthesia through a 2.8 mm clear corneal incision by surgeons masked to the groups, using AMO Sovereign Compact-WhiteStar System. We used 1.4% sodium hyaluronate (Healon GV, AMO) during capsulorhexis and IOL implantation. Surgical procedure involved creation of 2 sideports, capsulorhexis, hydrodissection and hydrodelineation, in-the-bag phacoemulsification usually using stop-and-chop technique, bimanual aspiration of remaining cortical lens material, capsular bag refilling with viscoelastic material, insertion of an injectable foldable acrylic intraocular lens in capsular bag and bimanual aspiration of the viscoelastic substance from the anterior chamber, retrolental space and the capsule fornix. Corneal incisions were sealed by hydration and anterior chamber was reformed with balanced salt solution. Finally, a subconjunctival injection of dexamethasone and gentamicin sulfate was applied.

Statistical Analysis

Statistical analysis was performed by using SPSS version 16.0. All variables were distributed normally and they were expressed as mean±standard deviation. Gender was compared with chi-square test. One-way ANOVA test was used for group comparisons. An overall p value of <0.05 was considered as a statistically significant result. When an overall significance was observed, pairwise post-hoc tests were performed using Bonferroni's test.

RESULTS

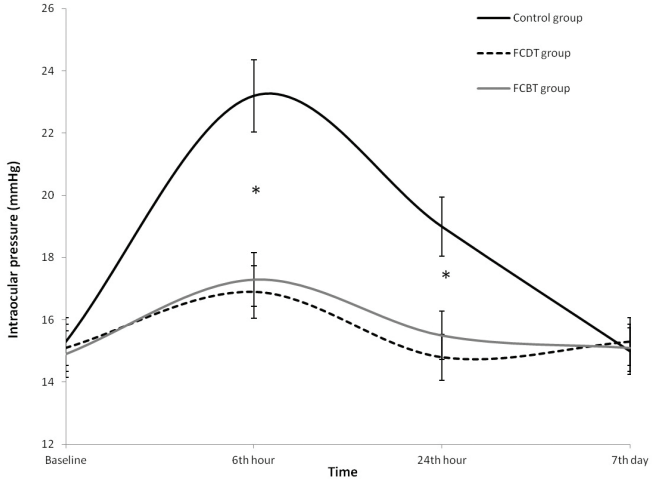
One hundred and forty seven patients (98%) completed the study. Three out of 50 patients (6%) in the control group were excluded from the study at 6th hour due to IOP elevations which were indication for exclusion. Demographic and clinical parameters of the groups are given in table. There were no statistically significant differences among the groups regarding age, sex and baseline IOP levels.

Table: *Demographic and clinical characteristics of the groups (mean±SD).*

Characteristic	FCDT group (n=50)	FCBT group (n=50)	Control group (n=47)	**P
Age (years)	67.2±8.5	68.8±7.5	66.5±8.6	0.350
Sex (Male/Female)	26/24	25/25	24/26	0.923
Mean IOP levels (mmHg)				
Baseline	15.1±2.2	14.9±2.2	15.3±2.3	0.622
6th Hour	16.9±3.0	17.3±3.3	23.2±5.0*	<0.001
24th Hour	14.8±2.1	15.5±2.2	19.0±2.7*	<0.001
7th Day	15.3±2.0	15.1±1.9	15.0±2.4	0.749
Mean IOP changes (mmHg)				
6th Hour	1.7±2.4	2.4±3.2	7.8±5.8*	<0.001
24th Hour	-0.3±1.6	0.6±2.9	3.6±3.3*	<0.001
7th Day	0.1±1.7	0.1±1.2	-0.3±2.0	0.163

FCDT; Fixed Combination Dorzolamide-Timolol, FCBT; Fixed Combination Brimonidin-Timolol, IOP; Intraocular Pressure
*Values causing statistically significant difference after pair-wise post-hoc tests.
**One-way ANOVA test.

Mean IOP levels were significantly lower in the treatment groups than in the control group at the 6th and 24th hours (both p<0.001) after surgery whereas there was no significant difference between the treatment groups during the follow-up period. On the other hand, mean IOP levels of study groups were similar at the 7th day. Additionally, when study groups were compared concerning the mean IOP rises from baseline, it was found that although both treatment groups had lower IOP rises than control group at 6th and 24th hours after surgery (both p<0.001) there was no significant difference between the treatment groups during the follow up period.



Graphic: *Mean intraocular pressure levels in the study groups during the study period.*
FCDT; fixed combination dorzolamide-timolol, FCBT; fixed combination brimonidine-timolol.
**p<0.001 treatment groups vs control group.*

There was no significant difference among the study groups regarding mean IOP changes from baseline at 7th day after surgery. Graphic shows mean IOP levels in the study groups during the study period.

DISCUSSION

This study demonstrated that one drop of either FCDT or FCBT administered immediately after surgery were similarly effective for preventing IOP spikes within 24 hours after phacoemulsification surgery. FCDT is a routinely used antiglaucomatous drug that consists of dorzolamide hydrochloride 2% and timolol maleate 0.5%.[13,14] Dorzolamide hydrochloride is an inhibitor of human carbonic anhydrase II. Inhibition of this enzyme in the ciliary processes of the eye decreases the secretion of aqueous humor and consequently reduces IOP by 10-20%.[15]

Timolol maleate is a nonselective beta adrenergic receptor blocking agent that inhibits aqueous humor secretion by about 50% and decreases IOP approximately 20-25%.[15]

On the other hand, FCBT is another combination eye drop that approved by FDA in 2007, containing brimonidine tartrate 0.2% and timolol maleate 0.5%. Brimonidine tartrate is an antiglaucomatous agent with alpha-2 selective adrenergic agonistic activity that lowers IOP by reducing aqueous humor production and enhancing uveoscleral outflow.[16]

IOP rises following phacoemulsification surgery have generally been reported in the early postoperative period.[2,17]

The pathogenesis of IOP elevation is unknown but it is probably multifactorial including damage to the trabecular meshwork, retained viscoelastic material, inflammatory cells and flare, hyphema, pupillary block and peripheral anterior synechiae.[17-19] However, previous studies that investigated medical prophylaxis of IOP elevation after cataract surgery are conflicting. Various antiglaucoma agents have been used to prevent transient IOP increases after cataract extraction, including oral and topical carbonic anhydrase inhibitors, intracameral cholinergic agents, topical beta blockers, apraclonidine, latanoprost brimonidine, whereas each drug had significant failure rates or limitations.[20-26]

The efficacy of FCDT for controlling IOP spikes after cataract surgery has been investigated previously.[13,17,26] Ozkurt et al.,[27] have compared the effects of FCDT with brimonidine for controlling IOP elevation after phacoemulsification surgery and they found that FCDT was more effective than brimonidine in reducing IOP 6 hours and 24 hours postoperatively. In another study, Rainer et al.,[14] investigated the effect of FCDT on IOP following cataract surgery with sodium chondroitin sulfate 4%-sodium hyaluronate 3% (Viscoat). They showed that although FCDT was effective in reducing IOP 6 hours and 20-24 hours after surgery, it did not prevent Viscoat-induced IOP spikes of 30 mmHg or higher.

In our study IOP spikes of 30 mmHg or higher were not observed in patients treated with FCDT. This may be caused by the different viscoelastic substance (1.4% sodium hyaluronate) that used in our study. In this regard, in another study[13] using sodium hyaluronate 1%, FCDT has been found to be more effective than latanoprost in reducing IOP after cataract surgery. They also displayed that FCDT was effective for preventing IOP spikes of 30 mm Hg or higher. On the other hand, to our best knowledge, this is the first time we evaluated the efficacy of FCBT for controlling IOP elevations after phacoemulsification surgery in comparison with FCDT.

Recently, FCDT and FCBT have been compared for treatment of glaucoma and ocular hypertension. Konstas et al.,[9] have compared the 24-hour efficacy of FCDT and FCBT in POAG and they demonstrated that each fixed combination significantly reduced IOP. However, FCDT had significantly better 24-hour efficacy than FCBT.

Yüksel et al.,[10] have evaluated the 6-month daytime efficacy of a FCBT versus FCDT as a first choice therapy in patients with PXG and shown that each fixed combination was effective to lower IOP. They also showed that daytime diurnal IOP was not statistically different when either FCDT or FCBT was used as a first choice therapy in these patients.

Another study investigating the efficacy and tolerability of the FCBT versus FCDT in patients with elevated IOP displayed that each fixed combination significantly reduced the mean diurnal IOP after 8 weeks of treatment.[11] There was no significant difference between FCDT and FCBT. In addition, Arcieri et al.,[12] have shown that FCDT and FCBT, each given twice daily, had similar efficacy in patients with POAG or ocular hypertension. In our study although FCDT was found to be more effective than FCBT for preventing IOP elevation after phacoemulsification surgery, the difference did not reach statistical significance. In conclusion, our study has demonstrated that both FCDT and FCBT, one drop administered immediately after procedure, were effective and both had similar efficacy for preventing IOP elevation after phacoemulsification surgery.

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