Comparison of Efficacy and Safety of Topical Dorzolamide-Timolol Maleate Combination with Oral Acetazolamide for Prevention of Intraocular Pressure Rise Following Phacoemulsification Surgery

Fakoemülsifikasyon Cerrahi Sonrası Göziçi Basınç Artışını Önlemede Topikal Dorzolamid-Timolol Maleat ile Oral Asetazolamidin Etkinlik ve Güvenilirlik Yönünden Karşılaştırılması

Servet ÇETİNKAYA,[a]
Nurullah AKÇAM,[a]
Tahir GÜRDAĞ,[a]
Yasemin Fatma ÇETİNKAYA[b]

[a]Clinic of Ophthalmology, Turkish Red Crescent Hospital, Konya
[b]Clinic of Ophthalmology, Atatürk Training and Research Hospital, Ankara

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Yazışma Adresi/*Correspondence:*
Servet ÇETİNKAYA
Turkish Red Crescent Hospital, Clinic of Ophthalmology, Konya, TÜRKİYE/TURKEY
drservet42@gmail.com

ABSTRACT Objective: To compare the efficacy and safety of topical dorzolamide-timolol maleate combination with oral acetazolamide for prevention of intraocular pressure rise following phacoemulsification surgery. **Material and Methods:** Sixty-seven eyes of 67 patients with cataracts (33 males, 34 females) who had undergone phacoemulsification and intraocular lens implantation surgery were evaluated retrospectively. Patients were divided into two groups. Group 1 comprised 33 (49%) patients who received oral acetazolamide 250 mg (Diazomid 250 mg tb) 1 hour before the surgery and 1hour after surgery and 125 mg 3 times a day for 3 days following surgery. Group 2 comprised 34 (51%) patients who received topical dorzolamide-timolol maleate combination 1 drop 1 hour before the surgery and twice a day for 3 days following surgery. **Results:** The mean preoperative intraocular pressure (IOP) of the first group was 14.60±3.21 standard deviation (SD) (range 10-21) mmHg. and that of the second group was 14.67±2.77 (SD) (11-21) mmHg (p=0.924). The mean postoperative IOP(1st day) of the first group was 15.27±2.90 (SD) (11-23) mmHg and that of the second group was 14.82±2.57 (SD) (11-23) mmHg (p=0.505). The mean postoperative IOP (1st week) of the first group was 13.72±2.44 (SD) (10-18) mmHg and that of the second group was 13.64±2.53 (SD) (10-19) mmHg (p=0.895). **Conclusion:** For prophylaxis of postoperative IOP rise after an uneventful cataract surgery, topical-dorzolamid timolol maleate combination and oral acetazolamide therapy have similar effects, however the adverse effects of systemic acetazolamide should be taken into account. Therefore it is better to prefer topical dorzolamide-timolol maleate combination therapy.

Key Words: Phacoemulsification; intraocular pressure; acetazolamide; dorzolamide-timolol combination

ÖZET Amaç: Fakoemülsifikasyon cerrahisi sonrası artan göziçi basıncını azaltmak için kullanılan ağızdan verilen asetazolamid ile damla şeklinde uygulanan dorzolamid-timolol maleat kombinasyonunun etkinlik ve güvenilirliğinin kıyaslanmasıdır. **Gereç ve Yöntemler:** Kataraktı olan ve fakoemülsifikasyon ve göziçi mercek (GİM) implantasyon cerrahisi geçiren 67 (33 erkek, 34 kadın) hastanın 67 gözü retrospektif olarak değerlendirildi. Hastalar iki gruba ayrıldılar. 1. grup 33 (%49) hastadan oluşmaktaydı, bu gruptaki hastalara ameliyattan 1 saat önce ve 1 saat sonra ağızdan 250 mg asetazolamid (toplam 500 mg) verildi ve ameliyattan sonraki 3 gün boyunca da 125 mg asetazolamid 3x1 önerildi. 2. grup 34 (%51) hastadan oluşmaktaydı, bu gruptaki hastalara ameliyattan 1 saat önce 1 damla dorzolamid-timolol maleat kombinasyonu uygulandı ve ameliyattan sonraki 3 gün boyunca da damla şeklinde dorzolamid-timolol maleat kombinasyonu 2x1 şeklinde önerildi. **Bulgular:** 1. grubun ortalama ameliyat öncesi göziçi basınç değeri 14,60±3,21 (SD) (10-21) mmHg idi, 2. grubunki ise 14,67±2,77 (SD) (11-21) mmHg idi (p=0,924).1. grubun ortalama ameliyat sonrası 1. gün göziçi basınç değeri 15,27±2,90 (SD) (11-23) mmHg idi, 2. grubunki ise 14,82±2,57 (SD) (11-23) mmHg idi (p=0,505). 1. grubun ortalama ameliyat sonrası 1. hafta göziçi basınç değeri 13,72±2,44 (SD) (10-18) mmHg idi, 2. grubunki ise 13,64±2,53 (SD) (10-19) mmHg idi (p=0,895). **Sonuç:** Komplikasyonsuz bir katarakt cerrahisi sonrası artabilecek olan göziçi basıncının kontrol altına alınabilmesi için proflaktik olarak kullanılan ağızdan verilen asetazolamid ile damla şeklinde uygulanan dorzolamid-timolol maleat kombinasyonu benzer etkilere sahiptir, ancak sistemik asetozolamidin yan etkileri düşünüldüğünde topikal dorzolamid-timolol maleat kombinasyonu tercih edilmelidir.

Anahtar Kelimeler: Fakoemülsifikasyon; intraoküler basınç; asetazolamid; dorzolamid-timolol kombinasyonu

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Viscoelastic substance maintains anterior chamber, protects the corneal endothelium, facilitates capsulorhexis and intraocular lens (IOL) implantation in cataract surgery.[1] However, when it is not removed completely, it may cause intraoculer pressure (IOP) rise within the first 24 hours following the cataract surgery.[2-5] There are also other causes which may contribute to elevated IOP after cataract surgery such as retained lens content, iris pigment release and hyphema caused by surgical trauma.[6]

Postoperative IOP rise may cause pain, discomfort, corneal edema, optic nerve damage and visual field loss in patients with preexisting glaucoma. Additionally, it may cause non-arteritic anterior ischaemic optic neuropathy, central retinal arterial or vein occlusion in susceptible patients.[1,6] Different agents like intracameral carbachol and acethylcholine, pilocarpine, beta-blockers, prostaglandin analoges, oral or topical carbonic anhydrase enzyme inhibitors may be used to prevent postoperative IOP spikes.[6-9]

In this study, we compared the efficacy and safety of topical dorzolamide-timolol maleate combination with oral acetazolamide for prevention of intraocular pressure rise following phacoemulsification surgery.

MATERIAL AND METHODS

The study protocol was approved by the local ethics commitee. An informed consent was obtained from the patients for the cataract surgery. The study was carried out according to the tenets of the Declaration of Helsinki.

In this study, 67 eyes of 67 patients with cataracts (33 males, 34 females) who had undergone phacoemulsification and IOL implantation surgery between January 2012 and June 2012 were evaluated retrospectively. Patients were divided into two groups. Group 1 comprised 33 (49%) patients who received oral acetazolamide 250 mg (Diazomid 250 mg tb) 1 hour before the surgery and 1 hour after surgery and 125 mg acetazolamide 3 times a day for 3 days following surgery, for a probable postoperative IOP rise. Group 2 comprised 34 (51%) patients who received topical dorzolamide-timolol maleate combination 1 drop 1 hour before the surgery and twice a day for 3 days following surgery, for a probable postoperative IOP rise again. The mean age of the patients was 62.52±10.45 (SD) (43-83) years. Full ophthalmological examinations were performed before the surgery and on 1st day, at 1st week, in 1st month, 3rd month, 6th month and 1st year following the surgery. Patients with glaucoma or any ocular or systemic diseases which might affect their vision and patients who had intraoperative complications like posterior capsule rupture and vitreous loss were excluded from the study. Preoperative IOP, postoperative 1st day's and 1st week's IOP measurements, preoperative best corrected visual acuities (BCVA) and postoperative (1st week) BCVA were compared between the groups and within the groups statistically.

All of the surgeries were performed by a single surgeon (SC). Under subtenon anesthesia, a 2.75 mm clear corneal incision was made. Anterior chamber was filled with a dispersive (hydroxypropylmethylcellulose, Easy Visc) viscoelastic substance. After continuous curvilinear capsulorhexis, hydrodissection and hydrodelineation was performed, then a sideport entrance was made. The nucleus was removed by using the "divide and conquer" technique (Sovereing Compact, AMO). The cortex was aspirated with coaxial irrigation/aspiration. The capsular bag was filled with a cohesive (Na Hyaluronate 1.6, Easyluron) viscoelastic substance. A foldable monofocal posterior chamber IOL (Acriva) was implanted in the capsular bag through an injector system. The viscoelastic material was aspirated completely as far as possible. The entrances were closed with stromal hydration. After surgery, patients used topical antibiotics 4x1 and topical steroids 6x1 for one week, and only topical steroids 4x1 daily for subsequent 3 weeks. Group 1 patients used oral acetazolamide 125 mg 3x1 and Group 2 patients used topical dorzolamide-timolol maleate combination 2x1 daily for 3 days.

The SPSS version 22 programme was used for statistical analysis. Data were compared between

the groups by using the Independent Samples t test and analysed within the groups by using the Paired t test and Chi-Square test. $p<0.05$ was accepted as significant.

RESULTS

In group 1, out of 33 patients, 17 were males (51%) and 16 were females (49%). In group 2, out of 34 patients, 16 were males (47%) and 18 were females (53%). The mean age of group 1 patients was 62.96±11.58 (SD) (46-83) years and the mean age of group 2 patients was 62.088±9.38 (SD) (43-81) years. In terms of age and gender there was no significant differences between two groups (p=0.733, p=0.720)

The mean preoperative BCVA of the first group was 0.83±0.21 (SD) (0.30-1.00) logMAR and that of the second group was 0.78±0.24 (SD) (0.4-1.00) logMAR, there was no statistically significant difference between two groups (p=0.312). The mean postoperative BCVA of the first group was 0.10±0.11 (SD) (0.00-0.30) logMAR and that of the second group was 0.07±0.11(SD)(0.00-0.030) logMAR. There was no statistically significant difference between two groups (p=0.411).

The mean preoperative IOP of the first group was 14.60±3.21 (SD) (10-21) mmHg and that of the second group was 14.67±2.77 (SD) (11-21) mmHg. There was no statistically significant difference between two groups (p=0.924). The mean postoperative IOP (1st day) of the first group was 15.27±2.90 (SD) (11-23) mmHg and that of the second group was 14.82±2.57 (SD) (11-23) mmHg. There was no statistically significant difference between two groups (p=0.505). The mean postoperative IOP (1st week) of the first group was 13.72±2.44 (SD) (10-18) mmHg and that of the second group was 13.64±2.53 (SD) (10-19) mmHg. There was no statistically significant difference between two groups (p=0.895). These characteristics and results were summarized in Table 1.

The mean postoperative BCVA was significantly higher than the mean preoperative BCVA value in both groups ($p<0.001$). The mean preoperative IOP value was not significantly different from the mean 1st day's postoperative IOP value (p=0.077). But the mean 1st week's postoperative IOP value was significantly lower than the mean preoperative IOP value ($p<0.001$), in both groups. In group 1,1 (3%) patient complained of headache

TABLE 1: Characteristics and outcomes of group I and group 2 patients

Characteristics, Outcomes		Group 1, n=33 (Oral Acetazolamide) Mean, Percentage, Range	Group 2, n=34 (Topical Dorzolamide-timolol maleate combination) Mean, percentage, Range	p value
Age (years)		62.96±11.58 (SD) (46-83)	62.88±9.38 (SD) (43-81)	0.733
Sex	Male	17(51%)	16(47%)	0.720
	Female	16(49%)	18(53%)	
Preoperative BCVA (logMAR)		0.83±0.21 (SD) (0.30-1.00)	0,78 ± 0,24 (SD) (0.4-1.00)	0.312
Postoperative BCVA (logMAR)		0.10 ± 0.11 (SD) (0.00-0.30)	0.07 ± 0.11 (SD) (0.00-0.30)	0.411
Preoperative IOP (mmHg)		14.60±3.21 (SD) (10-21)	14.67± 2.77 (SD) (11-21)	0.924
Postoperative IOP (1st day) (mmHg)		15.27±2.90 (SD) (11-23)	14.82 ± 2.57 (SD) (11-23)	0.505
Postoperative IOP (1st week) (mmHg)		13.72±2.44 (SD) (10-18)	13.64 ± 2.53 (SD) (10-19)	0.895

BCVA: Best Corrected Visual Acuity; IOP: Intraocular Pressure; SD: Standard Deviation.

and fatigue, 1 patient (3%) complained of polyuria, 2 (6%) patients complained of paraesthesia in the fingers and toes and 2 (6%) patients complained of nausea and vomiting. These were the side effects of oral acetazolamide. In group 2 patients, no adverse effect related to topical dorzolamide-timolol maleate combination was observed.

DISCUSSION

In order to minimize IOP rise following cataract surgery, prophylaxis is needed. Zamvar and Dhillon reported that, 37.4% of the surgeons routinely prescribed some form of medication for lowering IOP postoperatively, and the majority (86.8%) used oral acetazolamide.[10]

Carbonic anhydrase inhibitors (CAI) have been used to treat glaucoma since 1954. CAIs decrease aqueous humor synthesis by inhibiting carbonic anhydrase-isoenzyme II. Systemic CAIs are very effective in reducing IOP. However, they have many side effects including headache, dizziness, fatigue, confusion, convulsion, irritability, fever, paraesthesiae, nausea, vomiting, diarrhoea, loss of appetite, thirst, metabolic acidosis, polyuria, renal stone formation, skin rash, urticaria, and hypersensitivity reactions. Also, they may cause very rare but fatal reactions like anaphylactic reactions, Stevens-Johnson syndrome and aplastic anemia.[1,11-13] Dorzolamide and brinzolamide are two topical CAIs which are currently available to treat ocular hypertension and glaucoma. Dorzolamide is a very potent inhibitor of carbonic anhydrase-isoenzyme II. Its site of action is local within the eye, it decreases aqueous humor production thus leading to a decrease in IOP. Systemic side effects of topical dorzolamide are minimal; the most frequent one is a transient bitter taste. The most frequent ocular side effects of topical dorzolamide are burning and stinging.[13-18] The IOP lowering effect of dorzolamide is enhanced by combination of timolol maleate which is a beta-blocker.[14,19] In our study, we detected adverse effects of oral acetazolamide like headache, fatigue, polyuria, paraesthesia, nausea and vomiting. However, neither systemic nor ocular side effects were observed in patients who received topical dorzolamide-timolol maleate combination.

Topical CAIs (dorzolamide, brinzolamide) were found to be more effective, less effective and as effective as systemic acetazolamide, in different studies.[20-23] In our study, the effectiveness of dorzolamide-timolol maleate combination was not different from that of oral acetazolamide.

Rainer et al. reported that the fixed dorzolamide-timolol combination was effective in reducing IOP 6 hours and 20 to 24 hours after cataract surgery.[24] However, it did not prevent Viscoat-induced IOP spikes of 30 mmHg or higher. Hurber-van der Velden et al. reported that IOP reduction by a pure mechanical procedure like oculopression leads to a significant increase of flow velocities of the retrobulbar vessels.[25] This effect can significantly be increased by using dorzolamide prior to oculopression.

In conclusion, for prophylaxis of postoperative IOP rise after an uneventful cataract surgery, topical dorzolamide-timolol maleate combination and oral acetazoloamide therapy have similar effects. However the adverse effects of systemic acetazolamid should be taken into account, therefore it is better to prefer topical dorzolamide-timolol maleate combination therapy.

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