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Effects of topical dorzolamide on IOP after phacoemulsification with different types of ophthalmic viscosurgical devices

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PURPOSE. *To evaluate the effect of topical dorzolamide on postoperative intraocular pressure (IOP) after routine phacoemulsification surgery with different type of ophthalmic viscosurgical device (OVD).*

METHODS. *Patients who were scheduled for phacoemulsification with intraocular lens (IOL) implantation were evenly divided into four groups. Group I (83 eyes) received one drop of topical dorzolamide immediately after surgery and 1.4% NaHa (BD Visc®) was used as a cohesive OVD during IOL implantation. Group II (83 eyes) did not receive any topical antiglaucoma medication after operation and 1.4% NaHa was used as a cohesive OVD. Group III (83 eyes) received topical dorzolamide and 1% NaHa (Healon®) was used, and Group IV (83 eyes) did not receive any topical and 1% NaHa was used in operation. Mean postoperative IOPs were compared between groups.*

RESULTS. *Eyes with 1.4% NaHa usage (18.2±9.2 mmHg) had higher mean postoperative IOPs than eyes with 1% NaHa usage (15.5±5.3 mmHg) (p=0.002). Mean postoperative IOPs were lower in eyes with dorzolamide application (15.6±7.2 mmHg) than in eyes without any medication (18.1±8.5 mmHg) both in eyes with 1.4% NaHa and 1% NaHa usage (p=0.003). Dorzolamide application caused an average 2.5 mmHg decrease in mean postoperative IOPs in both groups.*

CONCLUSIONS. *Effects of OVDs on IOP rises after phacoemulsification surgery are closely related to their molecular structure. Increase in viscosity rendered higher postoperative IOP increments. However, topical dorzolamide application effectively reduced postoperative IOP increments in eyes with both Healon® and BD Visc® use. (Eur J Ophthalmol 2007; 17: 38-44)*

KEY WORDS. *Intraocular pressure, Ophthalmic viscosurgical device, Phacoemulsification, Topical dorzolamide*

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INTRODUCTION

Small incision cataract surgery and implantation of intraocular lens (IOL) is the preferred method of cataract surgery by most surgeons today (1-3). A major concern in the postoperative management of patients is a rise in intraocular pressure (IOP) that frequently occurs in the immediate postoperative period (4, 5). Fortunately, high pressure levels are often transient. Factors that cause IOP increase may include pupillary block, peripheral anterior synechiae, watertight suturing of the wound, and surgical damage to the trabecular meshwork. Inflammatory debris, hyphema, and retained ophthalmic viscosurgical device (OVD) may decrease the outflow facility of the anterior chamber by obstructing trabecular meshwork (2, 6-8).

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To prevent the postoperative IOP rise, rigorous removal of the OVD at the end of the surgery is necessary. In spite of meticulous aspiration of anterior chamber at the end of the surgery, the postoperative IOP levels were not in desirable limits for all patients and for all type of OVD. Therefore treatment with an antiglaucoma agent is recommended (1-5).

There is no published comparative research on evaluation for effect of dorzolamide on postoperative IOP rise in usage of different cohesive OVD having the same chemical integrity but different concentration, different molecular weight, and different viscosity. It causes these OVD to display different physical and rheologic properties.

In this prospective study we evaluated effect of topical dorzolamide on postoperative IOP after routine phacoemulsification surgery with different type of OVD.

METHODS

In this study, 332 eyes of 332 patients who were scheduled for phacoemulsification with IOL implantation were enrolled. The exclusion criteria were history of previous ocular surgery, glaucoma, known hypersensitivity to carbonic anhydrase inhibitors, corneal abnormality precluding applanation tonometry, and treatment with systemic drugs which might have secondary effects on IOP, such as beta blockers, acetozolamide, or other carbonic anhydrase inhibitors. All subjects were treated in accordance with the requirements of the Declaration of Helsinki.

All patients were outpatients and operated with the same surgical technique. Approximately 1 to 2 hours before surgery, diclofenac, tropicamide hydrochloride 1%, phenylephrine hydrochloride 2.5%, and cyclopentolate 1% eye drops were instilled. After sub-Tenon anesthesia with lidocaine, a clear corneal incision was performed. Anterior chamber was filled with Viscoat® (sodium chondroitin sulfate 4.0% and sodium hyaluronate 3.0%) for capsulorhexis. Hydrodissection and phacoemulsification of the nucleus were followed by aspiration of the cortical remnants and polishing of the capsular bag. The capsular bag was expanded either with 1% sodium hyaluronate (NaHa) (Healon® Pharmacia) or 1.4% sodium hyaluronate (BD Visc® Becton, Dickinson and Company) and IOL was implanted in the bag. Healon has a molecular weight of 4.0 million Dalton and 230,000 mPaS shear-zero viscosity whereas BD Visc has 5 to 6 million Dalton molecular weight and 4.8 million mPaS shear-zero viscosity (Tab. I). Both OVD were aspirated in a standardized fashion from retrolental space, the capsule fornix, retroiridal, prelental, and preiridal spaces, without approaching the endothelium too closely. Clear corneal main-port and side-port incisions were hydrated with balanced salt solution (BSS® Alcon) to attain watertight wound closure without any suture. Subconjunctival injections of antibiotic and steroid were administered at the end of operation.

A Goldmann applanation tonometer was utilized to measure IOP 1 day before surgery for evaluation of baseline level. The postoperative IOP was measured with the same tonometer at 7 o'clock the following morning. Postoperative IOP measurements were performed at most 20 hours after surgery.

TABLE I - CLASSIFICATION OF COMMON OPHTHALMIC VISCOSURGICAL DEVICES (OVD)

OVD	Concentration	MW (D)	V0 (mPaS)
Healon®	1.0% NaHa	4.0 M	230 K
BDVisc®	1.4% NaHa	5–6 M avg	4.8 M
BD MultiVisc®	2.5% NaHa	3.0 M avg	16.0 M
Healon GV®	1.4% NaHa	5.0 M	2.0 M
Microvisc®	1% NaHa	5.0 M avg	1.0 M avg
Microvisc Plus®	1.4% NaHa	6.0 M avg	3.3 M avg
Viscoat®	3.0% NaHa 4% CDS	500 K	41 K
Cellugel®	2.0% mod HPMC	100 K	28 K

MW (D) = Molecular weight (Daltons); V0 (mPaS) = Zero-shear viscosity (milliPascal seconds); NaHa = Sodium hyaluronate; M = Million; K = Thousand; avg = Average; CDS = Chondroitin sulfate; HPMC = Hydroxypropyl methylcellulose

Patients were evenly divided into four groups. Group I (83 eyes) received one drop of topical dorzolamide (Trusopt® dorzolamide hydrochloride sterile ophthalmic solution 2%, Merck, Whitehouse Station, NJ) immediately after surgery and 1.4% NaHa was used as a cohesive OVD during IOL implantation. Group II (83 eyes) did not receive any topical antiglaucoma medication after operation and 1.4% NaHa was used as a cohesive OVD. Group III (83 eyes) received topical dorzolamide and 1% NaHa was used, and Group IV (83 eyes) did not receive any topical and 1% NaHa was used in operation.

If postoperative IOP was 30 mmHg or higher, an additional antiglaucoma medication was applied. To calculate postoperative changes in IOPs, values of preoperative IOPs were subtracted from values of postoperative IOPs. IOPs higher than 22 mmHg were recorded for each group. Routine follow-up including best-corrected visual acuity, biomicroscopy, fundus evaluation, and IOP measurement was performed after surgery.

An analysis of variance (ANOVA) was used to compare the age and preoperative IOP differences between the groups. Postoperative IOPs and changes in IOP between preoperative and postoperative IOP were assessed by means of a 2 (between groups: dorzolamide application and no treatment) x 2 (between groups: 1.4% NaHa and 1% NaHa) model of two way analysis of variance. Pairwise group differences were tested using Student *t*-test. The distributions of frequencies of postoperative IOPs more than 22 mmHg, eyes with an additional antiglaucoma treatment were assessed with chi-square test. If a requirement for chi-square test was not met Fisher exact test was performed. p Value less than 0.05 was considered significant.

RESULTS

Demographic data of patients are shown in Table II. Groups had similar age and sex distribution. Difference between groups in regard to mean age was insignificant (p=0.789). Male to female ratios were not different between groups (p=0.777).

Table III shows the mean preoperative IOPs, mean postoperative IOPs, and mean change in IOP (postoperative IOP minus preoperative IOP) in each group. There was no significant difference between groups in regard to preoperative IOPs (p=0.056).

The mean postoperative IOPs of Group I (eyes with 1.4% NaHa and dorzolamide) (16.95±9.1 mmHg) was significantly lower than Group II (eyes with 1.4% NaHa and without dorzolamide) (19.43±9.7 mmHg) (p=0.031). But it was not significantly different between Group III (eyes with 1% NaHa and dorzolamide)

TABLE II - PATIENT DEMOGRAPHICS (N=332)

Groups	No. of cases	Mean age (years) ± SD	Men/women
Group I (1.4% NaHa and dorzolamide)	83	64.2±10.3	45/38
Group II (1.4% NaHa and without dorzolamide)	83	65.6±11.1	42/41
Group III (1% NaHa and dorzolamide)	83	65.6±11.8	41/42
Group IV (1% NaHa and without dorzolamide)	83	65.8±11.3	47/36

TABLE III - POSTOPERATIVE MEAN INTRAOCULAR PRESSURE (IOP) (mmHg)

Groups	Preoperative IOP ± SD (mmHg)	Postoperative IOP ± SD (mmHg)	IOP change IOP ± SD (mmHg)
Group I (1.4% NaHa and dorzolamide)	14.4±3.6	16.9±9.1	2.4±9.7
Group II (1.4% NaHa and without dorzolamide)	13.7±2.9	19.4±9.7	5.7±10.1
Group III (1% NaHa and dorzolamide)	15.2±3.0	14.3±5.0	–0.8±5.1
Group IV (1% NaHa and without dorzolamide)	14.3±3.2	16.8±8.9	2.4±9.3

(14.36±5.0 mmHg) and Group IV (eyes with 1% NaHa and without dorzolamide) (16.82±8.9 mmHg) (p=0.267).

Postoperative IOPs in Group I and Group III were not significantly different (p=0.287). Postoperative topical dorzolamide application significantly prevented significant postoperative IOP increase after phacoemulsification operation in eyes with 1.4% NaHa usage. The mean postoperative IOP in Group II was significantly higher than that of Group IV (p=0.033). IOPs increased significantly in eyes with 1.4% NaHa usage if postoperative dorzolamide was not applied.

Frequencies of eyes having IOPs more than 22 mmHg postoperatively were demonstrated in Table IV. Ratio of eyes having an IOP more than 22 mmHg was lower in Group I (12 eyes 14.4%) than Group II (24 eyes 28.9%). In addition this ratio was lower in Group III (9 eyes 10.8%) than Group IV (14 eyes 16.8%). Postoperative dorzolamide application was significantly effective for protection against immediate IOP rises with values more than 22 mmHg after both 1.4% NaHa and 1% NaHa usage. Ratio of IOP rise more than 22 mmHg was higher in Group II than Group IV. The risk of postoperative IOP spike is higher in 1.4% NaHa usage than in 1% NaHa usage.

Two way variance analysis showed that mean postoperative IOPs were lower in eyes with dorzolamide application (15.6±7.2 mmHg) than in eyes without any medication (18.1±8.5 mmHg) both in eyes with 1.4% NaHa and 1% NaHa usage (p=0.003). Dorzolamide application caused an average 2.5 mm decrease in mean postoperative IOPs in both groups. In addition eyes with 1.4% NaHa usage (18.2±9.2 mmHg) had higher mean postoperative IOPs than eyes with 1% NaHa usage (15.5±5.3 mmHg) (p=0.002) (Fig. 1).

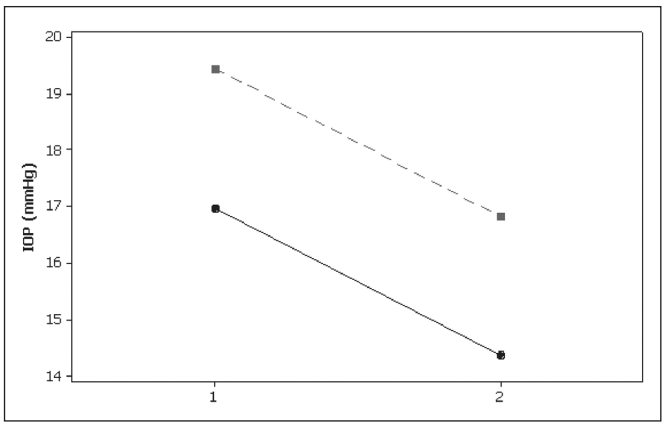

Fig. 1 - *The mean postoperative intraocular pressures (1 signifies 1.4% NaHa, 2 signifies 1% NaHa; line with squares at both ends shows eyes without dorzolamide and line with circles at both ends shows eyes with dorzolamide).*

The mean IOP increase was 2 mmHg in eyes with 1% NaHa usage and 7 mmHg in eyes with 1.4% NaHa usage without dorzolamide application.

The highest postoperative IOP was 52 mmHg in Group I, 55 mmHg in Group II, 30 mmHg in Group III, and 50 mmHg in Group IV. Nine eyes required an additional

TABLE IV - NUMBER OF EYES WITH AN INTRAOCULAR PRESSURE (IOP) OF 22 mmHg OR HIGHER AFTER SURGERY

	With dorzolamide	Without dorzolamide	Total
1.4% NaHa	12	24	36
1% NaHa	9	14	23
Total	21	38	59

TABLE V - NUMBER OF EYES WITH AN ADDITIONAL ANTIGLAUCOMA MEDICATION

	With dorzolamide	Without dorzolamide	Total
1.4% NaHa	9	11	20
1% NaHa	0	8	8
Total	9	19	28

Differences among groups statistically significant (Fisher's exact test) (p=0.029)

antiglaucoma medication in Group I, 11 eyes in Group II, no eyes in Group III, 8 eyes in Group IV (Tab. V). The difference between groups was significantly different (p=0.029). None of the eyes had an IOP of 50 mmHg with a flat or shallow anterior chamber. None of the patients had a drug related adverse event during the follow-up period.

DISCUSSION

An increase in postoperative IOP may be caused by different factors such as inflammation, hemorrhage, retained lens material, and the usage of OVD (9-11). Whatever the cause, clearance of OVD and retained materials by aspiration from the anterior chamber at the end of the surgery is highly recommended. Meticulous aspiration is effective in prevention of postoperative IOP elevation (9-12). However, many reports stress that even with appropriate aspiration of anterior chamber and elimination of OVD, the IOP elevation could be inevitable and it may only decrease IOP spike level or shorten its duration to the same extent (12, 13). Therefore various antiglaucoma agents have been used to prevent IOP increase after phacoemulsification surgery.

In our study we used dorzolamide hydrochloride 2%, which was a typical carbonic anhydrase inhibitor. Dorzolamide acts as an aqueous suppressant and it does not have any side effects such as bronchoconstriction, cardiac block, systemic hypertension, increased ocular inflammation, or CME. Dorzolamide does not have a direct action on uveoscleral and trabecular outflow.

Zohdy et al reported that the mean IOP was 19 mmHg in eyes receiving one drop of dorzolamide, 22 mmHg in eyes of subjects receiving acetazolamide 250 mg SR orally, and 27 mmHg in control group 4 hours after operation. They reported that the mean IOP were 19 mmHg, 17 mmHg, and 21 mmHg in each group respectively 24 hours after surgery. Their results indicate that both topical and systemic carbonic anhydrase inhibitors are effective in the prevention of early IOP rise following phacoemulsification. Our results were in accordance with these findings (4).

Rainer et al indicated that mean IOP was 19 mmHg in the dorzolamide, 22 mmHg in the latanoprost, and 48 mmHg in the control group 6 hours after operation. At 20 to 24 hours postoperatively the mean IOP changes were –0.9 mmHg in dorzolamide group, 0.3 mmHg in the latanoprost group, and 1.3 mmHg in control group, all of which received 1% NaHa as a OVD in the surgery (2). The results showed that both dorzolamide and latanoprost were effective in reducing the IOP increase at 6 hours after surgery but only dorzolamide was effective 20 to 24 hours postoperatively and these findings are very similar to our results. Because of hydration of corneal incisions at the end of surgery and outpatient based surgical practice, we could perform postoperative IOP measurements the next morning. Therefore we did not have any chance to assess IOP changes in the early postoperative period.

Rainer et al demonstrated that brimonidine 0.2% did not have any effect on reducing IOP after cataract surgery (2). According to Cetinkaya et al, prophylactic use of brinzolamide or brimonidine 1 hour before surgery did not effectively control postoperative IOP elevation (10).

In our study, the mean IOP increment was 2 mmHg in eyes with 1% NaHa usage and 7 mmHg in eyes with 1.4% NaHa usage if dorzolamide was not applied. Dorzolamide application caused an average 2.5 mm decrease in mean postoperative IOPs in both 1% NaHa and 1.4% NaHa usage. The mean IOP changes were significantly higher in 1.4% NaHa group than 1% NaHa group.

Although both of them consist of NaHa as a cohesive OVD, BD visc (1.4% NaHa) has different chemical and physical properties than Healon (1% NaHa). BD Visc consists of 1.4% NaHa and has higher molecular weight (5–6 million Dalton) and higher viscosity (4.8 million mPAS shear-zero viscosity). Healon consists of long chain 1% NaHa and its molecular weight is 4 million Dalton. Healon has a 230,000 mPAS shear-zero viscosity. The uneven difference between Healon and BD Visc is not only the NaHa concentration but these two OVD have different physical and rheologic properties causing dissimilar effects on postoperative IOP changes.

Arshinoff and Hofmann reported that postoperative IOP rise was not different between viscous OVD such as Healon (1% NaHa) and Microvisc (1% NaHa) (14). Also they reported in another study that the difference was not significant between Microvisc Plus® (1.4% NaHa) and Healon GV® (1.4% NaHa), both of which

were superviscous cohesive OVD. However they reported that postoperative mean IOPs were significantly lower in viscous group (Healon® and Microvisc®) than in the superviscous cohesive groups (Healon GV® and Microvisc Plus®) (15).

The reason for higher IOP elevation in eyes with high molecular weight OVD usage than low molecular weight OVD usage might be explained as follows. Low molecular weight substances are less viscous and they easily leave anterior chamber without causing a high increase in postoperative IOP. In contrast, high molecular weight substances are more viscous and they remain longer within the eye in an unmetabolized state and they disturb outflow facility by obstruction of trabeculum. Extrication of these high molecular weight substances from eye takes a longer time period than low molecular weight and less viscous OVD (9, 12, 16-18).

In conclusion, our study showed that effects of OVDs on IOP rises after phacoemulsification surgery are closely related to their molecular structure. Increase in viscosity rendered higher postoperative IOP increments. However, topical dorzolamide application effectively reduced postoperative IOP increments in eyes with both Healon and BD Visc use.

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