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ORIGINAL ARTICLE

A prospective, randomized clinical trial comparing the effects of three viscoelastics on the corneal endothelium after cataract surgery

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ABSTRACT

Objective

To compare the effects of Amvisc Plus (AP), Duovisc (DV), and Viscoat (VC) on the corneal endothelium of patients who have undergone uncomplicated phacoemulsification cataract surgery.

Methods

This is a prospective, randomized trial that involved 60 eyes of 48 patients with age-related cataracts. The eyes were randomly assigned to receive AP, DV, or VC during phacoemulsification. The main outcome measures were postoperative intraocular pressure (IOP), endothelial cell counts, and corneal thickness.

Results

The mean postoperative IOP were 15.13 ± 2.99 mmHg in the AP group, 15.42 ± 2.35 mmHg in the DV group, and 14.86 ± 5.56 mmHg in the VC group. The average postoperative endothelial cell counts were 2531 ± 420 cells/mm^2 in the AP group, 2330 ± 674 cells/mm^2 in the DV group, and 2678 ± 471 cells/mm^2 in the VC group. The mean postoperative corneal thickness measurements were 566 ± 49 m for the AP group, 561 ± 21 m for the DV group, and 552 ± 27 m for the VC group. No significant differences in all parameters were noted among the three groups.

Conclusion

The results of this study suggest that AP, DV, and VC may be comparable in terms of their ability to protect the corneal endothelium during phacoemulsification.

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PRIOR to the use of viscoelastic materials (VEMs), corneal edema was the most common cause of failed cataract surgery.[1] Postoperative corneal edema or corneal decompensation results from corneal endothelial damage during surgery.[2, 3] The introduction of VEMs in the 1970s greatly improved the outcome and safety of anterior segment surgery. The use of VEMs facilitates lens implantation by deepening the anterior chamber, protecting the corneal endothelium and iris surfaces from mechanical and thermal damage, and absorbing offending molecules on the surface of intraocular lenses (IOL).

VEMs are classified as being either cohesive or dispersive. Cohesive agents have high molecular weights and surface tension. They are primarily used to maintain the anterior chamber. Dispersive agents, meanwhile, have lower molecular weights and surface tension. They are primarily used to protect the corneal endothelium. Different VEM products and formulations have already been developed. These include sodium hyaluronate and chondroitin sulfate.[4-12]

Combining the use of cohesive and dispersive agents during surgery has been advocated by some authors.[13] While many previous studies have compared the protective abilities of other products, the authors of this study believe that this is the first simultaneous comparison of Amvisc Plus (AP) (1.6% sodium hyaluronate, Bausch & Lomb, Rochester, NY, USA), Viscoat (VC) (3% Na hyaluronate + 4% chondroitin sulfate, Alcon, Fort Worth, TX, USA), Duovisc (DV) (a dual system consisting of Viscoat and Provisc [1% sodium hyaluronate], Alcon, Fort Worth, TX, USA).

Parallel improvements in phacoemulsification techniques and instrumentation have also enhanced the safety and efficiency of cataract surgery. In the light of these advances, the authors conducted this study to determine whether the choice of VEM has a critical effect on endothelial cell count and corneal edema following cataract surgery.

METHODOLOGY

Adult patients from the University of the Philippines-Philippine General Hospital and the Asian Eye Institute who were scheduled to undergo phacoemulsification cataract surgery were prospectively enrolled in the study. Patients with a history of corneal pathology, corneal decompensation, trauma, glaucoma, and uveitis were excluded from the study. Also excluded were eyes with intraocular pressure (IOP) higher than 22 mmHg as measured via Goldmann's applanation tonometry, endothelial cell count of under 700 cells/mm^2, and corneal thickness of more than 650 m. Sixty eyes of 48 patients were included in the study.

Approval of the study protocol and informed consent forms were obtained from the Institutional Review Board of the two centers prior to the start of the study.

Measurements

All patients underwent a standard preoperative eye examination, which included history taking, visual acuity measurement, IOP measurement, and biomicroscopic examination of the anterior and posterior segments. The following data were collected in preoperative and postoperative periods: best corrected visual acuity (BCVA), IOP, central corneal thickness (CCT) as measured by ultrasonic corneal pachymetry (Pachette 2, DGH, Exton, PA, USA), and corneal endothelial cell density as measured by noncontact specular microscopy (SP1000, Topcon Corporation, Japan).

A single observer (KEB), masked as to which treatment group a patient belonged in, interpretsed specular microscopy results and determined the endothelial cell count. Masked observers measured visual acuity and IOP, as well as graded cataract nuclear density according to the Lens Opacities Classification System II (LOCS II).[14] There were no statistically significant differences in preoperative visual acuity, IOP, endothelial cell count, and corneal thickness among the three groups (Table 1).

Surgical Technique

At the time of surgery, the patients were randomly assigned to one of three VEM treatment groups using a random number generator. Twenty-two (36 %) of 60 eyes were assigned to receive AP, 19 (32 %)were assigned to receive VC, and 19 (32 %) were assigned to receive DV. Because of unique packaging and handling properties concerning the agents used, it was not possible to mask the surgeon as to which VEM was used.

All surgeries were performed by a single surgeon (HSU). Phacoemulsification was performed under topical anesthesia using proparacaine 0.5%. A side port was made with a 15-degree keratome. The assigned VEM was injected through the side port until the anterior chamber was filled. For eyes assigned to receive DV, the Viscoat component

Table 1. **Baseline preoperative characteristics of eyes within each viscoelastic material (VEM) group (N = 60 eyes)**

Parameter	Amvisc Plus	Duovisc	Viscoat	ANCOVA*
Visual acuity (decimal units)	0.32 ± 0.27	0.24 ± 0.21	0.24 ± 0.21	$p > 0.468$
IOP (mmHg)	15.58 ± 0.76	14.44 ± 0.74	14.00 ± 0.81	$p > 0.335$
Cell count (cells/mm^2)	2692.50 ± 545	2440.00 ± 610	2918.89 ± 299	$p > 0.05$
Corneal thickness (m)	546 ± 41	544 ± 34	544 ± 23	$p > 0.969$

*Analysis of covariance

was used to fill the anterior chamber. A clear corneal incision was made using a 3.2mm keratome. Continuous curvilinear capsulorrhexis was done, followed by hydrodissection and hydrodelineation with balanced saline solution. Phacoemulsification was performed using the same machine for all eyes (Legacy 2000, Alcon Laboratories, Fort Worth, TX, USA). Nuclear disassembly was performed using a stop-and-chop technique.

After removing the remaining cortical material using an irrigation and aspiration (I/A) probe, the anterior chamber and capsular bag were filled with viscoelastic. For the DV group, the Provisc component was used to fill the chamber prior to insertion of the IOL. All eyes were implanted with a foldable one-piece acrylic IOL. The VEM was removed using I/A until the anterior chamber was cleared of all visible VEM. The phacoemulsification time, ultrasound power, and total operative time were recorded (Table 2). The patients were examined on the first, eighth, and fifteenth days after the operation.

Statistical Analysis

An analysis of covariance (ANCOVA) model was used to evaluate differences in visual acuity, intraocular pressure, endothelial cell count and pachymetry after adjusting for patient factors, surgery time, phacoemulsification time, phacoemulsification power, gel type, nuclear sclerosis, and period of observation. Tukey's multiple comparison procedure was used to perform post-hoc analysis during the follow-up period. A significance level of 0.05 was used to test all hypotheses.

RESULTS

The mean patient age was 67 ± 12 years (Figure 1). Eighteen patients (37.5%) were male. Thirty-seven (70%) patients underwent single-eye surgery while the rest underwent bilateral surgery.

The main outcome measures included postoperative visual acuity, IOP, endothelial cell count, and corneal thickness (Table 3).

The mean visual acuity in decimal units on Day 15 were 0.75 ± 0.21 in the AP group, 0.74 ± 0.21 in the DV group, and 0.83 ± 0.25 in the VC group. Visual outcomes were not affected by the type of VEM used during surgery when other factors were kept constant ($p > 0.740$). Patient factors and period of follow-up demonstrated statistical significance in the differences in visual acuity ($p < 0.001$).

Post-hoc analysis using Tukey's method demonstrated that visual acuity significantly improved on Days 1, 4, 8, and 15 after surgery. From baseline, there was an average of 0.5 units (50%) of improvement on Day 1, 0.8 units (80%) of improvement by Day 8, and 0.4 units (40%) on Day 15. This suggests that the best improvement in vision after phacoemulsification was achieved between Day 1 and 8. The amount of visual improvement declined after Day 8 regardless of VEM used and phacoemulsification time and power.

The mean postoperative IOPs on the first postoperative day were 15.13 ± 2.99 mmHg in the AP group, 15.42 ± 2.35 mmHg in the DV group, and 14.86 ± 5.56 mmHg in the VC group. Postoperative IOP was not affected by the type of VEM used during surgery ($p > 0.347$). Surgical factors (phacoemulsification time and power, surgical duration) had no effect on IOP ($p > 0.206$). Only patient factors such as age and cataract density had an effect on IOP ($p = 0.007$). The model accounted for 59.2% of the variability in IOP.

The average endothelial cell counts on Day 15 were 2531 ± 420 cells/mm^2 in the AP group, 2330 ± 674 cells/mm^2 in the DV group, and 2678 ± 471 cells/mm^2 in the VC group (Table 4). Regardless of VEM type, analysis of within-

Table 2. **Cataract nuclear density grading and surgical parameters during phacoemulsification using three different VEMs (N = 60 eyes)**

Parameter	Amvisc Plus	Duovisc	Viscoat	ANCOVA*
Nuclear sclerosis	2.2 ± 0.8	2.4 ± 0.8	2.4 ± 0.8	$p > 0.50$
Phaco time (mins)	1.23 ± 0.66	1.41 ± 0.68	1.25 ± 0.71	$p > 0.41$
Phaco power (%)	15.82 ± 6.11	15.50 ± 3.49	14.16 ± 5.44	$p > 0.31$
Surgery duration (mins)	19.73 ± 6.48	21.47 ± 6.42	19.21 ± 5.55	$p > 0.26$

*Analysis of covariance

Table 3. **Postoperative characteristics of eyes within each VEM group (N = 60 eyes)****

Parameter	Amvisc Plus	Duovisc	Viscoat	ANCOVA*
Visual acuity (decimal units)	0.75 ± 0.21	0.74 ± 0.21	0.83 ± 0.25	$p > 0.740$
IOP (mmHg)	15.13 ± 2.99	14.42 ± 2.35	14.86 ± 5.56	$p > 0.335$
Cell count (cells/mm^2)	2531 ± 420	2330.00 ± 674	2678 ± 471	$p > 0.05$
Corneal thickness (m)	566 ± 49	561 ± 21	552 ± 27	$p > 0.992$

*Analysis of covariance
**Values measured on day 15 except IOP, which was measured on first postoperative day

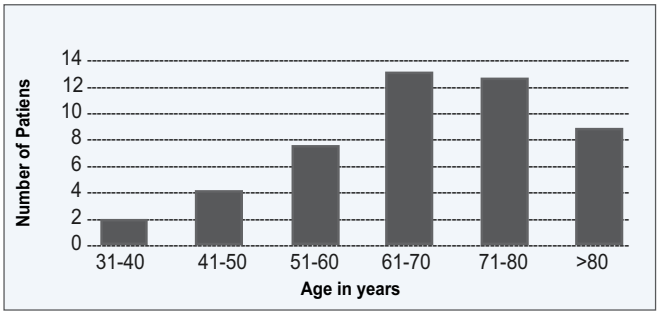

Figure 1. Age distribution of patients undergoing cataract surgery (n=48)

Table 4. **Preoperative and postoperative endothelial cell count (cells/mm²)**

VEM	Preoperative	Postoperative	Change (%)
Amvisc Plus	2692	2531	- 6.0
Duovisc	2440	2330	- 4.5
Viscoat	2919	2678	- 8.3

Table 5. **Preoperative and postoperative corneal thickness (mm)**

VEM	Preoperative	Postoperative	Change (%)
Amvisc Plus	546	566	+ 3.7
Duovisc	544	561	+ 3.1
Viscoat	544	552	+ 1.5

subjects effects showed a significant decrease in cell count, with a mean of 167 cells/mm², between baseline and Day 1.

Endothelial cell counts were not affected by type of VEM used during cataract surgery, when other independent variables were kept constant ($p > 0.05$). Phacoemulsification time ($p = 0.522$), power ($p = 0.631$), and surgical duration ($p = 0.143$) had no significant effect on endothelial cell count after surgery. However, patient factors, nuclear sclerosis, and follow-up period independently but significantly affected cell count ($p < 0.001$). The model accounted for 94.5% of the variability in cell count regardless of VEM type.

The mean corneal thickness measurements on Day 15 were 566 ± 49 m for the AP group, 561 ± 21 m for the DV group, and 552 ± 27 m for the VC group (Table 5). Postoperative corneal thickness measurements did not differ significantly among the VEM groups ($p > 0.992$). Postoperative corneal thickness was independent of phacoemulsification time ($p = 0.536$) and power ($p = 0.326$), surgical duration ($p = 0.996$), and nuclear sclerosis ($p = 0.286$). Patient factors and period of follow-up significantly affected postoperative corneal thickness ($p < 0.001$).

DISCUSSION

Endothelial cell loss is a primary indicator of corneal injury. Since endothelial cells do not regenerate, adjacent cells expand to fill in the gaps. As a result, endothelial cell density or count decreases and cell size increases in response to injury. Endothelial cell hexagonality and corneal thickness have been shown to increase as a result of corneal stress.[2, 3]

Corneal thickness is regulated partly by active transport of ions across endothelial cell membranes. Chemical, thermal, or mechanical insult that interferes with endothelial cell function may disturb its pump function, resulting in corneal edema.

VEMs are used to protect the corneal endothelium during anterior segment surgery. While several products are available, it is unclear which products provide the best protection. Numerous studies have compared the performance of cohesive and dispersive types of viscoelastics during phacoemulsification. However, these studies have yielded mixed results. It has been suggested that dispersive viscoelastics provide better coating and protection of the endothelium while the use of cohesive agents, which are more easily removed from the anterior chamber, results in a decreased frequency of postoperative IOP rise. Other reports suggest that dispersive and cohesive agents do not differ significantly in terms of endothelial cell protection and tendency to cause postoperative IOP rise.[6-12, 15-17]

Glasser et al.[6] and Probst et al.[15] found no significant differences in endothelial cell loss after phacoemulsification using either Amvisc Plus or Viscoat. These studies found that Viscoat has a higher likelihood of being retained during surgery and may confer better endothelial cell protection.

The necessity of removing VEM completely at the end of the surgery to prevent postoperative IOP rise has also been investigated.[15-17] Davis and coauthors compared AP, VC, and OcuCoat (Bausch & Lomb, Rochester, NY, USA) and found that postoperative visual acuity and corneal thickness were similar, no matter what VEM was used.[12]

It is possible that advances in phacoemulsification instrumentation and techniques may have sufficiently improved the safety and efficiency of cataract surgery such that the type of VEM used is of secondary importance. This belief is supported by a recent study by Kiss et al. It revealed similar changes in corneal edema and endothelial cell morphology, whether the VEM used during phacoemulsification was expensive or low-cost.[18]

The results of this study support the findings of Kiss et al., showing that similar corneal endothelial and IOP changes occur regardless of the VEM used. The results of this study also suggest that other factors, such as patient age and degree of nuclear sclerosis, may be important determinants affecting the way the corneal endothelium recovers from surgery. The process of endothelial damage is likely to be multifactorial in nature. Surgical skill and technique are also likely to be important factors in determining surgical outcomes.

While this study suggests that the type of VEM may not be critically important in most surgeries, it is possible that the type of VEM used may be important in selected situations such as in Fuchs's endothelial dystrophy as well as other instances where there is endothelial compromise. More studies are needed to determine whether any VEM offers additional safety advantages in these selected cases.

This study shows that the type of VEM used does not significantly affect postoperative IOP, endothelial cell count, and corneal thickness after uncomplicated phacoemulsification with foldable intraocular lens implantation.

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