A Prospective Randomized Study on the Role of Viscoadaptive OVD Healon5 Versus Combining Viscodispersive-Viscocohesive OVDs (Soft-Shell Technique) in Protecting the Corneal Endothelium During Phacoemulsification of Hard Cataract

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Abstract

Purpose: To evaluate the efficacy of the viscoadaptive OVD Healon5 in protecting the corneal endothelium during phacoemulsification of hard cataract as compared to using the dispersive-cohesive soft-shell technique in which the dispersive OVD Viscoat is combined with the cohesive OVD Provisc during surgery.

Methods: In this prospective randomized study, 30 eyes of 22 patients underwent phacoemulsification using either Healon5 (Group A, 15 eyes) or the dispersive-cohesive soft-shell technique (Group B, 15 eyes) with Viscoat and Provisc. All patients had age-related cataract, grades 3 and 4, with no other ocular pathology. Central corneal thickness (CCT) was examined preoperatively and at 1 and 7 days, as well as 1 month postoperatively. Corneal endothelial cell density (ECD) was examined preoperatively and 3 months postoperatively. The CCT and ECD were compared between the two groups.

Results: There was no statistically significant difference in the mean preoperative and the mean postoperative central corneal thickness between the two groups during any of the follow-up visits at 1 day, 7 days and 1 month postoperative. At 1 day postoperative, the mean increase in CCT in Group A was $64 \pm 6 \mu m$ while the mean increase in CCT in group B was $59 \pm 8 \mu m (p=0.076)$. At 7 days postoperative, the mean increase in CCT in Group A was $23 \pm 7 \mu m$ while in Group B it was $20 \pm 8 \mu m (p=0.302)$. After 1 month postoperatively, the mean increase in CCT was $2 \pm 4 \mu m$ and $3 \pm 1 \mu m$ for Groups A and B respectively ($p=0.452$). Such differences in the mean increase in CCT between both groups were statistically insignificant in any of the follow-up visits. Comparing endothelial cell loss after 3 postoperative months in the two groups, Group A had a $6.2 \pm 0.4\%$ cell loss while Group B showed $6.4 \pm 0.3\%$ cell loss. Such difference between the two groups was statistically insignificant ($p=0.072$).

Conclusion: The viscoadaptive agent Healon5 when utilized on its own is as effective as the dispersive cohesive soft-shell technique in protecting corneal endothelial cells during phacoemulsification of hard cataract.


Introduction

OPHTHALMIC viscosurgical devices (OVDs) are indispensable tools in modern cataract surgery. Their most important function during surgery is maintaining the anterior chamber and protecting ocular tissues, especially the corneal endothelium [1]. Arshinoff [2] has divided OVDs into two categories; viscohesive and viscodispersive.

A review of each of the OVD’s attributes should make it apparent that the use of a single agent during most ophthalmic intraocular procedures is accompanied by compromises in surgical suitability. In phacoemulsification for example, the ideal single OVD would offer a combination of cohesive and dispersive characteristics that would fulfill the range of needs through the course of the phacoemulsification procedure (Table 1 and Fig. 1).

In 1999, Arshinoff [5] proposed the soft-shell technique, which combines the use of the dispersive OVD Viscoat (sodium hyaluronate 3.0% – chondroitin sulfate 4.0%; Alcon Laboratories, Inc., Fort Worth, Texas, USA) and the cohesive OVD Provisc (sodium hyaluronate 1.0%; Alcon Laboratories, Inc., Fort Worth, Texas, USA). The introduction of the soft-shell technique helped characterize the differences between cohesive and dispersive OVDs. This dispersive-cohesive soft-shell technique greatly protects corneal endothelium because a dispersive agent is flattened by a cohesive agent to make a smooth layer adjacent to the corneal endothelium [6,7].
Table (1): Viscoelastic requirements during phacoemulsification [3].

<table>
<thead>
<tr>
<th>Surgical task</th>
<th>Viscoelastic function</th>
<th>Required properties</th>
<th>Agent category</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capsulorrhexis</td>
<td>Maintain deep anterior chamber</td>
<td>High viscosity at low shear rates; elasticity</td>
<td>Cohesive</td>
</tr>
<tr>
<td>Emulsify nucleus</td>
<td>Stay in eye to cushion and coat tissues, especially corneal endothelium</td>
<td>Low molecular weight; low surface tension; high viscosity at high shear rates</td>
<td>Dispersive</td>
</tr>
<tr>
<td>Remove cortex</td>
<td>Endothelial coating</td>
<td>Low surface tension</td>
<td>Dispersive</td>
</tr>
<tr>
<td>Open bag, insert IOL</td>
<td>Maintain deep anterior chamber and capsular bag</td>
<td>High viscosity at low shear rates; elasticity</td>
<td>Cohesive</td>
</tr>
<tr>
<td>Remove viscosurgical</td>
<td>Remove quickly and completely</td>
<td>High molecular weight; high surface tension</td>
<td>Cohesive</td>
</tr>
</tbody>
</table>

OVD regimens were evaluated in terms of their effect on central corneal thickness (CCT) and endothelial cell density (ECD) during the postoperative follow-up.

**Patients and Methods**

This is a prospective randomized study that involved 30 eyes of 22 patients undergoing cataract surgery at the International Eye Hospital, Cairo, Egypt during the period from October 2010 till June 2011. All surgeries were performed by the same surgeon (AES). Patients were divided into two groups:

- Group A involved 15 eyes undergoing phacoemulsification, using viscoadaptive OVD Healon5 (sodium hyaluronate 2.3%; Abott Medical Optics, Inc., Santa Ana, California, USA) as an OVD.
- Group B involved 15 eyes undergoing phacoemulsification by the soft-shell technique using cohesive OVD Provic (sodium hyaluronate 1.0%; Alcon Laboratories, Inc., Fort Worth, Texas, USA) and dispersive OVD Viscoat (sodium hyaluronate 3.0%–chondroitin sulfate 4.0%; Alcon Laboratories, Inc., Fort Worth, Texas, USA).

All patients provided informed consent before enrollment.

The inclusion criteria were age older than 45 years, age-related cataract grades 3 and 4, no other ocular pathology and pupil dilation greater than 7.0mm. Exclusion criteria were traumatic cataract, coexisting corneal endothelial disease, glaucoma, uveitis, pseudoexfoliation and previous ocular surgery.
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All surgeries were performed under topical anesthesia and were initiated with the creation of two 1.0mm paracenteses in clear cornea, followed by a 3mm clear corneal tunnel incision. Phacoemulsification was performed using the standardized stop-and-chop technique, in which an initial central groove was made into the nucleus during the sculpting phase extending as deep as \( \frac{3}{4} \) of the nuclear thickness. Then, the posterior nuclear plate was cracked bimanually. The chopping phase followed in which each heminucleus was chopped to smaller fragments and emulsified using the Neuhan chopper.

OVD injections were also standardized in both groups; the injections were given after the main incision was created, before phacoemulsification, and before the IOL implantation. In Group A, Healon5 was injected and the anterior chamber filled. In Group B (soft-shell technique), a small amount of Viscoat was injected filling \( \frac{1}{3} \) to \( \frac{1}{2} \) of the anterior chamber. The Provisc injection followed, starting beneath the Viscoat layer over the anterior capsule and slowly expanding and pushing the Viscoat layer towards the corneal endothelium until the anterior chamber was fully filled with a double layer OVD: Viscoat at the corneal end and Provisc at the anterior capsular end.

A Capsulorhexis was then created, and multi-quadrant hydrodissection and rotation were performed. Emulsification was performed with the Infiniti phaco machine (Alcon Laboratories, Inc., Fort Worth, Texas, USA), using standardized surgical parameters. Linear Torsional Phaco in continuous mode, with upper amplitude of 100%, together with activated Intelligent Phaco (IP) mode were utilized during the sculpting and chopping phases in both groups. The IP mode postulates that when a vacuum threshold of 80% of preset vacuum levels is reached, short pulses of longitudinal phaco are activated by the Infiniti machine. These short pulses of longitudinal ultrasound will help emulsification of hard fragments in a number of ways:

- These pulses will reposition the hard nuclear fragment in a better efficient plane away from the phaco tip, allowing a better shearing motion of torsional phaco for better emulsification. Torsional shearing motion acts best when the phaco tip is on the surface of the nuclear fragment rather than being embedded in it.
- Longitudinal ultrasound pulses help to emulsify the small hard fragments occluding the phaco tip. This prevents clogging of the tip by small fragments and reduces post-occlusion surge.

Longitudinal ultrasound pulses in IP mode were set at duration of 15msec for each pulse and at a ratio of 0.8 of the original preset maximum torsional amplitude. IP was set to work when 80% of preset vacuum level is reached. Linear vacuum upper limit was set at 100mmHG during sculpting and 450mmHG during chopping in both groups, with a flow rate set at 35ml/min.

After phacoemulsification, bimanual irrigation and aspiration (I/A) was done to ensure complete cortex removal. A Single piece AcrySof IOL (Alcon Laboratories) was implanted in the capsular bag, using a C cartridge with the Monarch II injector. The residual OVD was thoroughly removed by bimanual I/A. The rear surface of the IOL was elevated to remove the OVD trapped under the IOL.

Intraoperative energy utilized was noted in each case as measured by the cumulative dissipated energy (CDE). Ultrasound time (UST) represents the total time in seconds that U/S (or torsional-OZil) remained active. CDE correlates to the total amount of energy at the incision. CDE is calculated as follows:

For longitudinal phaco:

\[
CDE = \text{Average U/S power} \times \text{U/S time}
\]

In Torsional mode:

\[
CDE = \text{Torsional amplitude} \times \text{Torsional time} \times 0.4
\]

The frequency of the phaco tip in Torsional mode was 80% of the standard phaco (32kHz in Torsional versus 40kHz in longitudinal phaco), and the travel distance of the phaco tip in Torsional mode was half that in standard phaco. This helped justify setting the coefficient to 0.4. The ultrasound time (UST) and CDE values in Torsional and phaco mode were automatically calculated and displayed on the monitor of the phaco system.

Postoperatively, all eyes received topical Moxifloxacin and Prednisolone acetate eye drops which were given hourly on the first postoperative day and were tapered gradually over a period of 4 weeks.

The CCT was measured by ultrasound corneal pachymetry; preoperatively and at 1 day, 1 week and 1 month postoperatively. In each time, three acceptable values were generated, and a mean value was obtained. The corneal endothelium was evaluated using a non-contact specular microscope. The cells were analyzed for endothelial cell density (ECD), which was measured preoperatively and 3 months after surgery.
The nuclear opacity in all eyes was classified and only cases of nuclear grades 3 and 4 were assigned.

**Statistical analysis:**

For quantitative variables, mean and standard deviation (SD) were computed as summary statistics. The unpaired $t$-test was used to compare preoperative and postoperative parameters between the two groups. A $p$-value of less than 0.05 was considered significant. SPSS (version 17.0) statistical software was used for data analysis.

**Results**

The patients’ characteristics and intraoperative parameters in each group are shown in Table (2). There were no statistically significant differences in nuclear grade, ultrasound time or CDE between the two groups.

Table (2): Patient characteristics and intraoperative surgical system parameters.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Healon5 (Group A)</th>
<th>Softshell technique (Group B)</th>
<th>$p$-value *</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of eyes</td>
<td>15</td>
<td>15</td>
<td>NA</td>
</tr>
<tr>
<td>Age (years)</td>
<td>$68\pm8$</td>
<td>$72\pm7$</td>
<td>NA</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>9</td>
<td>8</td>
<td>1.000†</td>
</tr>
<tr>
<td>Female</td>
<td>6</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Parameter</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean nuclear grade</td>
<td>$3.6\pm0.5$</td>
<td>$3.73\pm0.5$</td>
<td>1.000*</td>
</tr>
<tr>
<td>Mean cumulative dissipated energy CDE</td>
<td>$15.8\pm1.6$</td>
<td>$15.6\pm0.5$</td>
<td>0.667*</td>
</tr>
<tr>
<td>Mean ultrasound time UST (sec)</td>
<td>$45.5\pm2.2$</td>
<td>$45.1\pm1.5$</td>
<td>0.552*</td>
</tr>
</tbody>
</table>

Mean±SD * Unpaired $t$-test † Chi-square test

Table (3) and Charts (1A,1B) show the mean preoperative and postoperative CCT by the two groups. There was no statistically significant difference in the mean CCT between the two groups preoperatively ($p=0.695$). There was no statistically significant difference of CCT in the postoperative period at 1 day, 7 days and 1 month between the two groups ($p=0.065, 0.233, 0.408$ respectively).

As shown in Table (3) and Charts (2A,2B), the mean increase in postoperative CCT showed no statistically significant values between the two groups in any of the follow-up visits. At 1 day postoperatively, the mean increase in CCT had a $p$-value of 0.076. At 7 days postoperatively, the mean increase in CCT had a $p$-value of 0.302. At the 1-month postoperative follow-up, the CCT had returned to its preoperative level with a mean increase of $2\pm4$ for the Healon5 Group and $3\pm1$ for the Soft-Shell Group ($p=0.452$). Such values were considered statistically insignificant.

Table (3): Mean preoperative and postoperative changes in CCT.

<table>
<thead>
<tr>
<th>Parameter: Mean central corneal thickness CCT ($\mu m$)</th>
<th>Healon5 (Group A)</th>
<th>Softshell technique (Group B)</th>
<th>$p$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative</td>
<td>$531\pm4$</td>
<td>$527\pm5$</td>
<td>0.695</td>
</tr>
<tr>
<td>1 Day postoperative</td>
<td>$595\pm4$</td>
<td>$590\pm7$</td>
<td>0.065</td>
</tr>
<tr>
<td>7 Days postoperative</td>
<td>$554\pm5$</td>
<td>$552\pm6$</td>
<td>0.233</td>
</tr>
<tr>
<td>1 Month postoperative</td>
<td>$555\pm4$</td>
<td>$534\pm5$</td>
<td>0.408</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Parameter: Mean increase in central corneal Thickness CCT ($\mu m$)</th>
<th>Pre-op Day 1 Day 7 1 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Day postoperative</td>
<td>$64\pm6$ $59\pm8$</td>
</tr>
<tr>
<td>7 Days postoperative</td>
<td>$23\pm7$ $20\pm8$</td>
</tr>
<tr>
<td>1 Month postoperative</td>
<td>$2\pm4$ $3\pm1$</td>
</tr>
</tbody>
</table>

Mean±SD * Unpaired $t$-test

Chart (1A&B): Mean preoperative and postoperative CCT.
There was no statistically significant difference in preoperative and 3 months postoperative ECD in both groups (p=0.382 and 0.121 respectively). The change in the mean endothelial cell density (ECD) in the two groups can be seen in Table (4) and Chart (3). The percentage of endothelial cell loss after 3 months in group A was 6.2±0.4% and in group B was 6.4±0.3%. The difference between the two groups was not statistically significant (p=0.072).

Table (4): Mean preoperative and postoperative ECD.

<table>
<thead>
<tr>
<th>Parameter: Mean endothelial cell density ECD (cells/mm²)</th>
<th>Healon5 (Group A)</th>
<th>Softshell technique (Group B)</th>
<th>p value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative</td>
<td>2598±21</td>
<td>2591±23</td>
<td>0.382</td>
</tr>
<tr>
<td>3 Months Postoperative</td>
<td>2438±21</td>
<td>2425±24</td>
<td>0.121</td>
</tr>
</tbody>
</table>

Discussion

At every stage of a cataract procedure the surgeon has options that can optimize corneal endothelial safety. After cataract surgery, endothelial cell loss ranges from 4% to 25% in most cases [10]. In patients followed for 10 years after cataract surgery, a study found that endothelial cell loss continued at a rate of 2.5% each year; four times the physiological annual rate [11]. While it is phacoemulsification and ophthalmic viscosurgical devices that have made modern cataract surgery possible, the choice of OVD used in cataract procedures can also influence the risk of acute endothelial cell loss [12].

Since their introduction in 1972, ophthalmic viscosurgical devices (OVDs) have revolutionized the way cataract surgery is performed and become essential tools for the anterior segment surgeon. They were first utilized to maintain space in the eye during the implantation of intraocular lenses. With the development of different types of OVDs, the number of available products continues to increase and improve, along with their functions during cataract surgery. They create and maintain anterior chamber depth and visibility, as well as protect the corneal endothelium and other intraocular tissues during surgery. OVDs minimize interaction between tissues and instruments and, therefore, ensure high tissue integrity [13-15].

In an attempt to help to understand their role in cataract surgery, Arshinoff 2 has divided OVDs into two categories as follows:

- ViscoCohesive OVDs are characterized by high-viscosity materials, which adhere to themselves...
through intramolecular bonds, or intermolecular entanglement and resists breaking apart. In general, OVDs with long molecular chains will be more cohesive because the molecules become entangled. Cohesive OVDs possess a high molecular weight, a high degree of pseudoplasticity and high surface tension.

- Visco Dispersive OVDs, exhibit opposite characteristics. They possess lower viscosity and adhere well to external surfaces, e.g., tissues and instruments. These materials tend to break apart easily compared to cohesive materials, exhibit lower molecular weight, lower surface tension and lower pseudoplasticity [2].

With the introduction of Healon5 (sodium hyaluronate 2.3%; Abbott Medical Optics, Inc., Santa Ana, California, USA), a new descriptive term was introduced; viscoadaptive. This term refers to the ability of an OVD to adapt its behavior to the intended surgical task without the surgeon having to do anything except perform the task at hand. Unlike devices that fit one or the other of the above categories, the viscoadaptive agent ideally functions as both, adapting its behavior to a changing parameter in its environment. That changing parameter under most circumstances is the degree of turbulence present [3] (Fig. 2).

![Fig. (2): Healon5’s response to turbulence](image)

To take advantage of the varying properties of cohesive and dispersive OVDs, the soft-shell technique (SST) was developed, which uses two very different viscoelastics in the same procedure. Arshinoff described the soft-shell technique, as a way to use two viscoelastic agents simultaneously. The dispersive OVD is placed first to coat the corneal endothelium, then the cohesive OVD is injected centrally to flatten the anterior lens capsule, deepen the anterior chamber, and force the dispersive OVD towards the cornea [8]. A 2003 survey of the American Society of Cataract and Refractive Surgery (ASCRS’s 2003 survey) showed that this technique using Viscoat and Provisc (sodium hyaluronate 1%; Alcon Laboratories, Inc.) was used by 37% of respondents [16,17].

In a study involving 57 patients with hard cataracts (Emery-Little classification grade 3 or higher), corneal endothelial cell loss after phacoemulsification was only 6.4% with the soft-shell technique using viscodispersive Viscoat and visco-cohesive Healon (sodium hyaluronate 1%; Abbott Medical Optics, Inc., Santa Ana, California, USA), compared to 16.3% using Healon alone (p=0.0003) [18]. There was also a transient increase in corneal thickness at day one after using Healon alone, while corneal thickness remained stable after using the soft-shell technique [18]. Another study, involving 230 cataract patients, yielded similar findings. It showed that in eyes with cataracts grade 4 endothelial cell loss was only 12.2% using the soft shell technique with Viscoat and Hyal-2000, compared to around 20% or more using Viscoat, Provisc or Hyal-2000 alone [19]. Use of the soft-shell technique in grades 3 and 4 cataracts reduced the amount of endothelial cell loss after 3 months making a 6.4% cell loss compared to 16.3% with the use of a single OVD [18,19].

Many studies have been published on the role of the soft-shell technique in endothelial protection, none of which have ever reported that the dispersive-cohesive soft-shell technique is inferior to either a dispersive or cohesive OVD on its own [20].

On the other hand, the characteristics of the viscoadaptive substances, such as Healon5, can be exploited to provide complete endothelial protection, prevent capsular breaks and ensure perfect IOL centration [21]. Healon5 is a long fragile chain, high molecular weight, super viscous substance that breaks at high shear rates. It is well retained in the eye and maintains space during high shear manipulations, but is also easily fractured so that it can coat well. However, complete removal of Healon5 is essential to prevent postoperative pressure upsurges. If regular Healon can be left in small quantities, not exceeding 20%, according to several studies, Healon5, which is 2.3 times more concentrated, should never exceed 7% [22].

Several studies compared Healon5 to other OVDs in terms of influence on endothelial cells. In a prospective randomized study on 74 eyes, comparing Healon5 with other various OVDs,
endothelial cell loss after cataract surgery with Healon5 was 6.2% 90 days postoperatively. This was significantly lower than the means in the other 4 groups \((p=0.002)\). In addition, two other studies show that Healon5 lead to a lower cell loss of 112 cells/mm² compared with super viscous cohesives \([22,23]\).

In terms of endothelial protection in cataract surgery, as shown in published literature, both Healon5 and the soft-shell technique are superior to either a cohesive or a dispersive agent on its own. An ideal OVD should be able to create and maintain space during intraocular surgical manipulation and should protect the corneal endothelium, i.e. have both cohesive and dispersive characteristics \([24,25]\). Therefore, in this prospective randomized study we examined the efficacy of employing a viscoadaptive OVD on its own in comparison with using both a dispersive and a cohesive agent together in the soft-shell technique in protecting corneal endothelium during phacoemulsification.

In this study, corneal endothelial cell loss and the increase in CCT did not differ statistically between the viscoadaptive OVD and the dispersive-cohesive soft-shell technique. These parameters were also similar in a study by Praveen M and his colleagues to compare the effects and outcomes of DisCoVisc, another viscoadaptive OVD (Alcon Laboratories), with those of the soft-shell technique (using Viscoat and Provisc) in phacoemulsification \([23]\). In their results, there was no significant difference in the mean endothelial cell loss 3 months after surgery or in the mean increase in CCT at 1 day and 7 days postoperatively \([23]\), which is consistent with findings in this study.

**Conclusion:**

In conclusion, a viscoadaptive OVD utilized on its own is as effective as the dispersive-cohesive soft-shell technique in protecting corneal endothelial cells during phacoemulsification of hard cataract. Our findings suggest that either Healon5 or the combined use of Viscoat and Provisc in soft-shell technique is superior to one another in protecting the corneal endothelium and that both OVD regimens provide additional protection to surrounding ocular tissues.

**References**


