

Safety and effectiveness of a new ophthalmic viscosurgical device: randomized, controlled study



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Purpose: To evaluate the safety and effectiveness of a new dispersive ophthalmic viscosurgical device (OVD) (ClearVisc) compared with an approved dispersive OVD (Viscoat) when used in cataract surgery.

Setting: 16 clinics in the United States.

Design: Prospective multicenter controlled randomized 1:1 (ClearVisc:Viscoat; stratified by site, age group, and cataract severity). Patients and examiners masked.

Methods: Patients aged 45 years or older with age-related non-complicated cataract considered amenable to treatment with standard phacoemulsification cataract extraction and intraocular lens (IOL) implantation were included. Patients were randomized to receive either ClearVisc or Viscoat using standard techniques. 5 postoperative visits occurred at 6 hours, 24 hours, 7 days, 1 month, and 3 months. The primary effectiveness outcome was the change in endothelial cell density (ECD) from baseline to 3 months. The primary safety end point was the proportion of patients who experienced at

least 1 intraocular pressure (IOP) measurement ≥ 30 mm Hg at any follow-up visit. Noninferiority was tested. Inflammation and adverse events were evaluated.

Results: 372 patients were randomized: 184 patients in the ClearVisc group and 188 patients in the Viscoat group. ClearVisc was noninferior to Viscoat in mean percentage of ECD loss from baseline to 3 months (8.4% and 6.8%, respectively). ClearVisc was significantly noninferior to Viscoat in the proportion of patients with postoperative IOP ≥ 30 mm Hg at any follow-up visit (17.4% and 20.3%, respectively, $P = .0002$).

Conclusions: ClearVisc dispersive OVD provides surgeons with a new option in the continuum of approved dispersive OVDs with beneficial properties as a surgical aid in cataract extraction and IOL implantation.

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During cataract surgery, phacoemulsification may cause damage to corneal endothelial cells through excessive ultrasound energy, collision of nuclear fragments with the corneal endothelium, movement of air bubbles, and localized increase in temperature.¹ One of the most damaging factors to the corneal endothelium is phacoemulsification-induced free radical generation, which causes oxidative insult to endothelial cells and cell death.^{1–5} The damaged endothelial cells cannot regenerate. The production of free radicals is increased in conditions such as a hard nucleus because phacoemulsification duration is prolonged.^{2,6} Although ophthalmic viscosurgical devices (OVDs) were originally developed to maintain space in the eye during surgery, they are now additionally used to protect the cornea to improve visual rehabilitation postoperatively.⁷

The terms cohesive and dispersive represent physical qualities that generally characterize OVDs. A cohesive OVD is easier to completely remove from the eye at the end of surgery, which reduces the likelihood of sudden increases in intraocular pressure (IOP) attributed to residual OVD obstructing the aqueous drainage system. However, a cohesive OVD may be unintentionally removed during the normal irrigation/aspiration associated with phacoemulsification and potentially result in less chamber stability and reduced protection for intraocular structures. Conversely, a highly dispersive OVD will maintain better levels of chamber stability and provide endothelial coating but may take longer to remove completely at the end of surgery. Nevertheless, for longer procedures, additional OVD may be needed because OVD may be aspirated from the eye and the protective effect of the OVD agent may be lost.^{1,8} Safety

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concerns typically associated with OVDs include an increase in IOP from retained OVD, inflammatory reactions, toxic anterior segment syndrome, and vision loss associated with increased IOP and inflammation.

Many marketed OVDs contain sodium hyaluronate (SH), a free radical scavenger.^{2,9} The scavenging benefits of SH are dependent on the retention of the OVD in the anterior chamber.^{1,8,10} In vitro, greater free radical scavenging occurs when the OVD contains more than 1 polymer, which creates a synergistic effect, for example, when an OVD contains both SH and sorbitol.² Sorbitol can also improve extrusion force and suppress clogging of the cannula when the same syringe is used repeatedly during surgery.⁸

ClearVisc OVD (SH 2.5%, Bausch & Lomb, Inc.) is a newly approved dispersive OVD. The intended purpose is to protect intraocular tissues during anterior segment surgery. ClearVisc is indicated for use as a surgical aid in ophthalmic anterior segment procedures including cataract extraction and intraocular lens (IOL) implantation.¹¹ ClearVisc was developed to provide both mechanical and chemical protection: the specific molecular weight and viscosity mechanically protect the corneal endothelium while both sorbitol and SH chemically protect the corneal endothelium.¹¹ The combination of sorbitol and SH demonstrate significantly higher free radical scavenging activity when compared with other commercially available dispersive OVDs in laboratory studies.²

This report describes the results of 2 studies: a clinical study and an ex vivo study. The purpose of this multicenter, masked, randomized, prospective clinical study was to assess the safety and effectiveness of ClearVisc when compared with Viscoat dispersive OVD (sodium chondroitin sulfate-SH, Alcon Laboratories, Inc.). Viscoat was chosen as the control because it has been used in cataract surgery for more than 20 years and has a proven safety record. Surgeon preference and visualization through the OVDs were assessed with an ex vivo study.

METHODS

Clinical Methods

Study Design and Patients This was a prospective, multicenter, randomized, masked, controlled study conducted at 16 sites in the United States. The surgeon was not masked to the OVD. A delegated examiner at each site who was masked to the randomized assignment performed all postoperative assessments. The study protocol was reviewed and approved by an Institutional Review Board in accordance with the tenets of the Declaration of Helsinki and the International Council for Harmonization Guideline for Good Clinical Practice. All patients provided written informed consent, and HIPPA regulations were followed. The study was registered on www.clinicaltrials.gov (NCT03511638).

Inclusion criteria were adults aged 45 years or older with age-related noncomplicated cataract considered amenable to treatment with standard phacoemulsification extraction and IOL implantation, with clear intraocular media other than cataract, and who provided written informed consent. Key exclusion criteria in the operative eye were as follows: corneal, anterior segment, or retinal pathology; baseline endothelial cell density (ECD) <1500 cells/mm²; Grade 4+ nuclear cataract density; glaucoma or ocular hypertension (IOP >24 mm Hg); use of any medication that may interfere with vision or complicate surgery; a

history of chronic or recurrent inflammatory eye disease; corrected distance visual acuity (CDVA) ≥ 1.0 logMAR in the fellow eye; and previous corneal surgery or retinal detachment.

Surgical Procedure and Follow-up At the time of surgery, patients were randomly assigned to receive either ClearVisc or Viscoat (control) in a 1:1 ratio stratified by site, age group, and cataract severity. Only 1 eye of each patient was included in the study. Two syringes of ClearVisc and Viscoat were provided in 1.0 mL and 0.75 mL quantities, respectively, to ensure that there was sufficient volume to complete each case. The OVD was typically instilled into the anterior chamber using standard aseptic technique prior to capsulorhexis and again prior to IOL implantation. The OVD may also have been used to coat the tips of surgical instruments and/or the IOL prior to implantation. The same OVD was used throughout each procedure. At the end of the surgical procedure, the OVD was removed from the eye as completely as practical by thoroughly irrigating and aspirating with a sterile irrigating solution. OVD volume used was assessed. No prophylactic ocular hypotensive medication was allowed during the study. Five postoperative visits were scheduled (6 hours, 24 hours, 7 days, 1 month, and 3 months). IOP measurements were obtained using a calibrated Goldmann Applanation Tonometer in accordance with manufacturer's instructions. Calibration of the Goldmann Tonometer was required at least monthly.

Outcome Measures and Data Analysis The primary effectiveness end point was a test for noninferiority of ClearVisc in mean percentage of ECD loss (the change from baseline to 3 months) when compared with Viscoat. ECD was assessed using a noncontact Specular Microscope (Konan Medical, Inc.). Three images from the central part of the cornea were obtained at each visit by certified staff. The reading center was masked to the OVD each patient received. Standardized ECD count methods were used to minimize variability.¹² Based on the results of a previous clinical trial that also used Viscoat as the control, the common standard deviation was assumed to be 14.2%.¹³ If the upper confidence limit of the difference in mean endothelial cell loss was <5%, then the null hypothesis of inferiority for the primary effectiveness end point was rejected in favor of the alternative hypothesis of noninferiority.

Safety was assessed through the monitoring of IOP, intraocular inflammation (anterior chamber cell and flare), and adverse events (AEs) during all postoperative visits. Measurement of aqueous cell and flare utilized the Standardization of Uveitis Nomenclature Working Group grading system.¹⁴ The primary safety variable was the proportion of patients who experienced at least 1 IOP measurement ≥ 30 mm Hg in the study eye at any follow-up visit. The secondary safety variables were mean changes from baseline in IOP at the 6-hour and at the 24-hour postoperative visits. Other safety assessments included manifest subjective refraction, CDVA, dilated fundus examination, ultrasound pachymetry, and slitlamp examinations. The incidence of patients who experience at least 1 IOP observation ≥ 30 mm Hg with Viscoat was estimated to be 0.117 (11.7%) based on the incidence range of postsurgical IOP spikes ≥ 30 mm Hg reported in studies evaluating Viscoat without prophylactic ocular hypotensive medication.¹⁵⁻¹⁷ A doubling of the control OVD incidence would be considered clinically significant; thus, the noninferiority margin was defined as equal to the expected rate. Therefore, for the primary safety end point, if the upper 95% confidence limit of the difference in incidence between groups was <0.117, the null hypothesis of inferiority was rejected in favor of the alternative hypothesis of noninferiority. The secondary null hypotheses were eligible for rejection only if both primary end points were met. The nominal alpha risk was 0.025 for the 1-sided secondary superiority hypothesis tests.

Assuming independence of the primary end points, the overall power of the study was calculated as 89.36% based on 93.90% and 95.17% power to reject the effectiveness and safety null hypotheses, respectively. To allow for a dropout rate of up to 10%, a

sample size of approximately 184 patients per treatment arm (368 patients total) was targeted for enrollment.

Continuous and categorical variables were summarized with descriptive statistics and counts and percentages. Data were analyzed using SAS (v. 9.4, SAS Institute, Inc.). All eyes with successful IOL implantation were included in the all-implanted analysis set (effectiveness analysis set). The safety analysis set included all eyes exposed to either OVD. The intent-to-treat population included all randomized eyes.

Ex Vivo Study

Porcine eyes were prepared by removing the corneal epithelium and were then mounted on a fixture for positioning under the surgical scope. Six qualified cataract surgeons performed standard cataract surgeries using ClearVisc or Viscoat, 3 times each. During the surgery, the surgeons graded the performance of each OVD (1 = excellent to 5 = unacceptable) against an attribute list. Data were averaged and summarized.

RESULTS

Clinical

Three hundred seventy-two patients were randomized in the study, of which 184 patients were in the ClearVisc group and 188 patients were in the Viscoat group. Discontinuation occurred for 2 patients in the ClearVisc group (1 lost to follow-up and 1 withdrew consent) and 1 patient in the Viscoat (withdrew consent). A total of 182 patients (98.9%) in the ClearVisc group and 187 patients (99.5%) in the Viscoat group completed the study.

Both groups had similar demographics and baseline characteristics (Table 1). Most patients were White (262/372 patients, 70.4%); the mean age was 69.4 years, and 231 patients (62.1%) were women. The cataract was classified as combination for 57.5% (214/372) of patients and nuclear for

39.5% (147/372) of patients, and density was moderate (2+) or dense (3+) for 96.2% (358/372) of the cataracts.

All surgical parameters were similar between the groups (Table 2). Adequate pupil dilation was maintained in all eyes. All lens material, including cortex, was completely removed from 100% (184/184) of the ClearVisc group and 98.8% (186/188) of the Viscoat group. All OVD was removed from the anterior chamber and capsular bag of 100% (184/184) of the ClearVisc group and 99.5% (187/188) of the Viscoat group. Two syringes of OVD were provided for each case. Compared with the Viscoat group, the ClearVisc group used a lower estimated percentage volume from the first syringe of OVD and used a lower estimated total percentage volume including both syringes. The ClearVisc group had a larger percentage of patients using only 50% of the total volume compared with the Viscoat group (52.7% vs 34.6%, respectively) and a smaller percentage of patients using 75% or 100% of the volume (25.0% vs 31.9% and 19.6% vs 29.8%, respectively).

Primary Outcomes

The ClearVisc group had a mean percentage of ECD loss of 8.4% from baseline to 3 months, whereas the Viscoat group had a mean percentage of loss of 6.8% (Figure 1), with a least square mean difference (LSMD; test – control) of 1.6% between the groups (90% CI, –0.5 to 3.6). Thus, ClearVisc was noninferior to Viscoat in mean percentage of ECD loss ($P = .0032$).

The proportion of patients with postoperative IOP ≥ 30 mm Hg at any follow-up visit was 0.174 for the ClearVisc group and 0.203 for the Viscoat group (difference

Table 1. Demographics and baseline characteristics (safety analysis set)

Parameter	ClearVisc (N = 184)	Viscoat (N = 188)	Total (N = 372)
Age (y), n (%)			
Mean (SD)	69.6 (6.76)	69.2 (7.37)	69.4 (7.07)
Range	47, 86	45, 86	45, 86
Sex, n (%)			
Male	73 (39.7)	68 (36.2)	141 (37.9)
Female	111 (60.3)	120 (63.8)	231 (62.1)
Race, n (%)			
White (Caucasian)	124 (67.4)	138 (73.4)	262 (70.4)
Asian	39 (21.2)	43 (22.9)	82 (22.0)
Black or African American	20 (10.9)	7 (3.7)	27 (7.3)
American Indian/Alaskan Native	2 (1.1)	2 (1.1)	4 (1.1)
Other	1 (0.5)	0	1 (0.3)
Cataract classification, n (%)			
Nuclear	75 (40.8)	72 (38.3)	147 (39.5)
Cortical	4 (2.2)	4 (2.1)	8 (2.2)
Posterior subcapsular	1 (0.5)	2 (1.1)	3 (0.8)
Combination	104 (56.5)	110 (58.5)	214 (57.5)
Density slight (1+)	9 (4.9)	4 (2.1)	13 (3.5)
Density moderate (2+)	86 (46.7)	102 (54.3)	188 (50.5)
Density dense (3+)	88 (47.8)	82 (43.6)	170 (45.7)
Density very dense (4+)	1 ^a (0.5)	0	1 (0.3)

Percentages are calculated as (n/N) × 100

^aAn exclusion criterion states that a Grade 4+ nuclear cataract density is exclusionary; however, this patient's cataract type was cortical, so the patient was deemed eligible for the study.

Table 2. Surgical procedure (safety analysis set)

Parameter	ClearVisc (N = 184)	Viscoat (N = 188)
Effective phacoemulsification time (s), n	183	188
Mean (SD)	10.6 (13.59)	12.4 (19.60)
Min, max	0, 78	0, 178
Phacoemulsification system pump		
Venturi, n (%)	76 (41.3)	74 (39.4)
Peristaltic, n (%)	108 (58.7)	114 (60.6)
OVD removal flow rate (mL/min), n	164	165
Mean (SD)	45.9 (13.59)	45.8 (13.21)
Min, max	22, 60	22, 60
OVD removal vacuum level (mm Hg), n	129	135
Mean (SD)	605.9 (85.79)	600.4 (94.69)
Min, max	88, 713	88, 715
Total time to remove OVD (min), n	184	188
Mean (SD)	0.99 (0.430)	1.00 (0.405)
Min, max	0.3, 2.7	0.1, 2.6
Incision location		
Cornea, n (%)	163 (88.6)	165 (87.6)
Sclera, n (%)	21 (11.4)	23 (12.2)
Incision size (mm), n	184	188
Mean (SD)	2.56 (0.258)	2.55 (0.258)
Min, max	1.8, 2.8	1.8, 2.8
Estimated total volume of OVD used in the first syringe		
25%	5 (2.7)	7 (3.7)
50%	97 (52.7)	65 (34.6)
75%	46 (25.0)	60 (31.9)
100%	36 (19.6)	56 (29.8)
Estimated total volume of OVD used in the second syringe		
0%	175 (95.1)	172 (91.5)
25%	2 (1.1)	7 (3.7)
50%	5 (2.7)	7 (3.7)
75%	2 (1.1)	2 (1.1)
100%	0	0

Percentages are calculated as (n/N) × 100

estimate [test – control] = -0.029 ; 90% CI, 0.096-0.038). Thus, ClearVisc was significantly noninferior to Viscoat in the proportion of patients with postoperative IOP ≥ 30 mm Hg at any follow-up visit ($P = .0002$). The comparison is significantly noninferior means that the comparison met the hypothesis test for noninferiority as described in the Methods section. Five patients in the Viscoat group and 4 patients in the ClearVisc group had an IOP > 30 mm Hg on 2 consecutive visits. A subgroup analysis of patients with postoperative IOP ≥ 30 mm Hg demonstrated that ClearVisc was non-inferior to Viscoat for patients who received IOP-reducing intervention (difference estimate = -0.074 ; 90% CI, -0.208 to 0.060; $P = .0095$) and for patients who did not receive IOP-reducing intervention (difference estimate = 0.005; 90% CI, -0.026 to 0.036; $P < .0001$).

Secondary Outcomes

At 6 hours, the ClearVisc and Viscoat groups had a similar mean change from baseline in IOP (9.4 mm Hg and 10.0 mm Hg, respectively), with an LSMD (test – control) of -0.4 mm Hg between the groups (95% CI, -2.0 to 1.1) (Figure 2). Similarly, at 24 hours, the ClearVisc and Viscoat groups had a similar mean change from baseline in IOP (4.1 mm Hg and

3.9 mm Hg, respectively), with an LSMD (test – control) of 0.3 mm Hg between the groups (95% CI, -0.8 to 1.3). Thus, ClearVisc was not superior to Viscoat at 6 hours ($P = .3013$) or 12 hours ($P = .2990$).

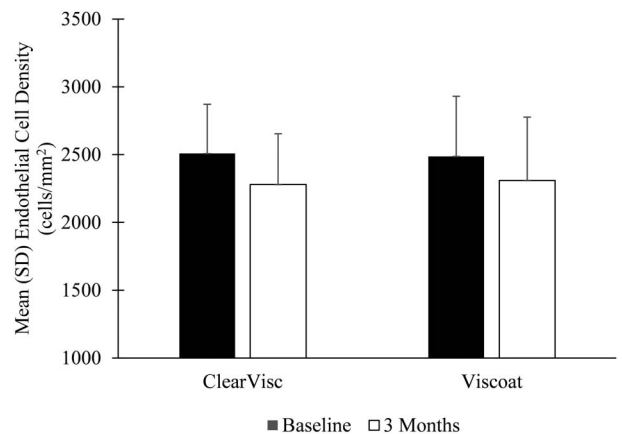


Figure 1. Mean loss of endothelial cell density (cells/mm²) from baseline to 3 months: intent-to-treat population. The 1.6% difference in percent loss met noninferiority criteria.

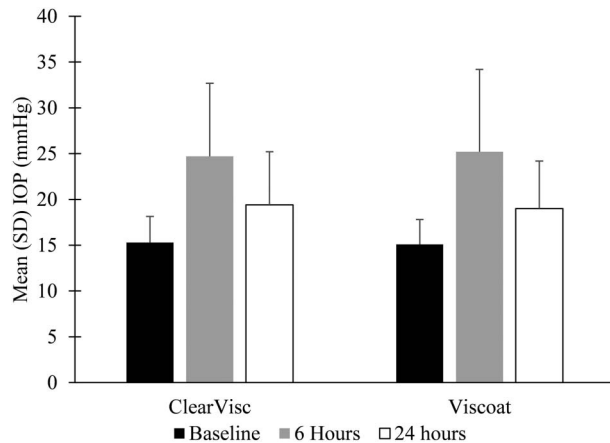


Figure 2. Mean IOP (mm Hg) over time: safety population. Superiority criterion was not met.

Adverse Events

A total of 100 AEs were reported for 64 patients (34.8%) in the ClearVisc group and 122 AEs were reported for 83 patients (44.1%) in the Viscoat group (Table 3). Most (>93%) of the AEs were mild or moderate in severity. Severe AEs were reported for 4 patients (6 events) in the ClearVisc group (punctate keratitis, corneal edema, increased IOP, hyphema, acute respiratory failure, and chronic obstructive pulmonary disease) and 2 patients (2 events) in the Viscoat group (corneal edema and aortic aneurysm). There were 30 adverse device effects (ADEs, related to the device) in the ClearVisc group and 34 ADEs in the Viscoat group. The most common ADE was IOP increase, with similar percentages in the ClearVisc and Viscoat groups (13.6% and 16.5%, respectively). All other ADEs were reported for 1 patient in either group. There was 1 serious ADE (posterior capsule rupture in an eye treated with Viscoat).

The proportion of patients reporting an AE at least once was similar across groups (Table 4). Of the most common

AEs, the most frequently reported ($\geq 5\%$ of patients in either group) were increased IOP (16.8% and 20.2% for ClearVisc and Viscoat, respectively) and punctate keratitis (9.2% and 6.9% for ClearVisc and Viscoat, respectively).

There were no device malfunctions, use errors, or difficulties with use. Intraoperative capsular tear, zonular tear, or vitreous loss were reported for 1 eye in the ClearVisc group and 4 eyes in the Viscoat group.

Other Observations Related to Safety

The mean CDVA was 0.29 ± 0.2 logMAR for both groups at baseline. By 3 months, the mean CDVA improved to 0.05 ± 0.1 logMAR for both groups. The results of post-operative slitlamp examination were similar between groups for presence/severity of corneal stromal edema, presence/severity of corneal wound edema, number of anterior chamber cells, and presence/severity of anterior chamber flare. The percentage of patients who had an abnormal dilated fundus examination was similar between groups at baseline (ClearVisc: 34.2%, 63/184; Viscoat: 30.9%, 58/188) and at 3 months (ClearVisc: 36.3%, 66/182; Viscoat: 32.6%, 61/187). The mean corneal thickness was similar between groups at baseline (ClearVisc: $555.2 \mu\text{m}$, Viscoat: $556.9 \mu\text{m}$) and at 3 months (ClearVisc: $552.8 \mu\text{m}$, Viscoat: $555.1 \mu\text{m}$). In eyes with ClearVisc, clear corneas (no or mild stromal edema) were observed in 90.6% (164/181) at 24 hours, 99.5% (182/183) at 7 days, 100% (183/183) at 30 days, and 100% (182/182) of eyes at 3 months. Similarly, in eyes with Viscoat, clear corneas were observed in 92.0% (172/187) at 24 hours, 98.4% (182/185) at 7 days, 100% (187/187) at 30 days, and 100% (187/187) of eyes at 3 months.

Ex Vivo

The data of 6 surgeons were pooled across 9 wet-lab surgical procedures. In general, both products were rated good to

Table 3. Overall summary of AEs (safety population)

No. (%) of patients reporting at least 1	ClearVisc (N = 184)		Viscoat (N = 188)	
	n (%)	Total events	n (%)	Total events
AE	64 (34.8)	100	83 (44.1)	122
AE by severity ^a				
Mild	36 (19.6)	60	52 (27.7)	88
Moderate	24 (13.0)	34	29 (15.4)	32
Severe	4 (2.2)	6	2 (1.1)	2
AE by relationship to study device ^b				
Unrelated	37 (20.1)	70	49 (26.1)	88
Related	27 (14.7)	30	34 (18.1)	34
SAE	1 (0.5)	2	4 (2.1)	5
SAE by relationship to study device ^b				
Unrelated	1 (0.5)	2	3 (1.6)	4
Related (ADE)	0	0	1 (0.5)	1
Related and unanticipated (UADE)	0	0	0	0
AE leading to death	0	0	0	0
AE leading to study discontinuation	0	0	0	0

ADE = adverse device effect; AE = adverse event; SAE = serious adverse event; UADE = unanticipated adverse event

^aPatients reporting more than 1 AE were counted only once using the highest severity

^bPatients reporting more than 1 AE were counted only once using the closest relationship to study device

Table 4. Most common treatment-emergent AEs (reported for $\geq 1\%$ of patients in either group by preferred term: safety population)

System organ class/preferred term ^a	ClearVisc (N = 184), n (%)	Viscoat (N = 188), n (%)
Total number of AEs	100	122
Patients reporting at least 1 AE	64 (34.8)	83 (44.1)
Eye disorders	41 (22.3)	50 (26.6)
Punctate keratitis	17 (9.2)	13 (6.9)
Posterior capsule opacification	7 (3.8)	6 (3.2)
Iritis	6 (3.3)	5 (2.7)
Conjunctival hemorrhage	4 (2.2)	4 (2.1)
Eye inflammation	3 (1.6)	3 (1.6)
Posterior capsule rupture	1 (0.5)	5 (2.7)
Corneal edema	2 (1.1)	3 (1.6)
Vitreous floaters	1 (0.5)	4 (2.1)
Foreign body sensation in eyes	2 (1.1)	2 (1.1)
Blepharitis	2 (1.1)	1 (0.5)
Conjunctivitis allergic	0	3 (1.6)
Corneal disorder	3 (1.6)	0
Eye irritation	1 (0.5)	2 (1.1)
Macular fibrosis	1 (0.5)	2 (1.1)
Cystoid macular edema	2 (1.1)	0
Investigations	33 (17.9)	38 (20.2)
Intraocular pressure increased	31 (16.8)	38 (20.2)
Injury, poisoning, and procedural complications	3 (1.6)	9 (4.8)
Cataract operation complication	0	5 ^b (2.7)
Corneal abrasion	2 (1.1)	3 (1.6)

AE = adverse event; MedDRA = Medical Dictionary for Regulatory Activities

^aAEs not related to a device were coded to System Organ Class and Preferred Term using the MedDRA, v. 20.0

^bTorn posterior capsule. Two of these events were considered serious; both resulted in vitreous loss and retained lens material, and 1 required pars plana vitrectomy with lensectomy and membrane stripping.

excellent for all attributes, except Viscoat had worse ease of OVD removal from the anterior chamber (scored acceptable to poor). Ranking the scores showed that ClearVisc performed slightly better than Viscoat on 6 of 11 tested attributes, including visualization, IOL delivery, chamber maintenance, ease of removal, overall performance, and overall comparison. Both OVDs had a high surgeon rating of visualization of ocular tissue through OVD; however, air bubbles were observed with Viscoat and not with ClearVisc.

DISCUSSION

Viscosity, elasticity, and cohesion are important OVD physical properties, which alter retention and removal properties and may affect the surgeon's choice of OVD.^{18,19}

The selection of an OVD can also be influenced by individual patient anatomy and preexisting medical conditions and by individual surgeon technique and preferences. Dispersive OVDs are associated with a transient increase in IOP and an increased risk for postoperative inflammatory reactions. Phacoemulsification cataract surgery is associated with endothelial cell loss.²⁰ Thus, parameters commonly used in clinical trials to assess the performance of OVDs are IOP spikes to measure how completely the OVD is removed from the eye at surgery completion, inflammatory reactions, and ECD changes to evaluate how effectively the OVD forms a protective coating over the corneal endothelium. In this study, the incidence of transient increases in IOP ≥ 30 mm Hg with ClearVisc was low (17.4%) and noninferior to Viscoat

(20.3%). Note, prophylactic ocular hypotensive medication was prohibited, which may explain the incidence of pressure spikes. The incidence of inflammatory reactions (anterior chamber cells and flare and AEs of eye inflammation) was similar between treatment groups. Moreover, ClearVisc was noninferior to Viscoat in mean percentage loss of ECD from baseline. Thus, the primary effectiveness and safety end points were met. The ex vivo data and other research demonstrate that the benefits of ClearVisc use are similar to those of other dispersive OVDs, in that ClearVisc creates and maintains space during lens extraction and IOL implantation, aids in tissue manipulation during surgery, enhances visualization during the surgical procedure, and protects the corneal endothelium and other intraocular tissues.²¹

ClearVisc is unique in that it contains both SH and sorbitol; this combination helps control free radical damage.² Furthermore, sorbitol can help with extrusion of the OVD from the syringe.⁸ The ClearVisc syringe includes a larger volume of OVD (1.0 mL) compared with the Viscoat syringe (0.75 mL), resulting in a lower frequency in use of the total syringe volume in the ClearVisc group. The use of a second syringe is associated with an increased cost and delays in the operating room.

After cataract surgery, surgical trauma causes early rapid loss of ECD, and the rate of loss decreases over time.^{20,22} The study follow-up was 3 months. This study duration was selected because it is the minimum period adequate for detecting effects of surgical trauma that lead to a change in

ECD and is therefore the minimum period acceptable for studies evaluating an ECD end point. It is expected that the greatest ECD loss would occur within the study duration. A strength of this study is the prospective, masked, multicenter design evaluating a large number of patients, surgeons, and clinics. Limitations of this study are that surgeon OVD preference and macular edema were not assessed during the clinical trial. Moreover, the performance of the OVDs were not evaluated in situations of very dense cataracts, endothelial dystrophies, or postcorneal transplant phacoemulsification.

Together, the clinical and ex vivo studies demonstrate that ClearVisc creates and maintains space during lens extraction and IOL implantation, aids in tissue manipulation during surgery, enhances visualization during the surgical procedure, and protects the corneal endothelium and other intraocular tissues. ClearVisc may also be used to coat IOLs and instruments during ophthalmic anterior segment surgical procedures.¹¹ Thus, ClearVisc dispersive OVD provides surgeons with a new option in the continuum of approved dispersive OVDs with beneficial properties as a surgical aid in cataract extraction and IOL implantation.

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WHAT WAS KNOWN

- Ophthalmic viscosurgical devices (OVDs) were originally developed to maintain space in the eye during surgery; they are now additionally used to protect the cornea to improve visual rehabilitation postoperatively.

WHAT THIS PAPER ADDS

- ClearVisc OVD was developed to provide both mechanical and chemical protection of the corneal endothelium.
- The safety, effectiveness, and use of ClearVisc are comparable with those of a dispersive OVD with demonstrated safety and effectiveness.
- ClearVisc dispersive OVD provides surgeons with a new option with beneficial properties as a surgical aid in cataract extraction and IOL implantation.

REFERENCES

1. Takahashi H. Corneal endothelium and phacoemulsification. *Cornea* 2016; 35(suppl 1):S3–S7
2. Mauger F, Maltese A, Ward KW, Bucolo C. Hydroxyl radical scavenging activity of a new ophthalmic viscosurgical device. *Curr Eye Res* 2007;32: 105–111
3. Holst A, Rolfsen W, Svensson B, Ollinger K, Lundgren B. Formation of free radicals during phacoemulsification. *Curr Eye Res* 1993;12:359–365
4. Rubowitz A, Assia EI, Rosner M, Topaz M. Antioxidant protection against corneal damage by free radicals during phacoemulsification. *Invest Ophthalmol Vis Sci* 2003;44:1866–1870
5. Takahashi H. Free radical development in phacoemulsification cataract surgery. *J Nippon Med Sch* 2005;72:4–12
6. Badoza D, Fernandez Mendy J, Ganly M. Phacoemulsification using the burst mode. *J Cataract Refract Surg* 2003;29:1101–1105
7. Bissen-Miyajima H. In vitro behavior of ophthalmic viscosurgical devices during phacoemulsification. *J Cataract Refract Surg* 2006;32:1026–1031
8. Watanabe I, Nagata M, Matsushima H. Addition of D-sorbitol improves the usability of ophthalmic viscosurgical devices. *Clin Ophthalmol* 2019;13: 1877–1885
9. Artola A, Alio JL, Bellot JL, Ruiz JM. Protective properties of viscoelastic substances (sodium hyaluronate and 2% hydroxymethylcellulose) against experimental free radical damage to the corneal endothelium. *Cornea* 1993; 12:109–114
10. Takahashi H, Suzuki H, Shiwa T, Sakamoto A. Alteration of free radical development by ophthalmic viscosurgical devices in phacoemulsification. *J Cataract Refract Surg* 2006;32:1545–1548
11. ClearVisc 2.5% Sodium Hyaluronate Directions for Use. Bridgewater, NJ: Bausch & Lomb, Inc.; 2021
12. ISO 11979-1:2018 Ophthalmic implant—intraocular lenses
13. Healon Endocoat Oviscosurgical Ophthalmic Device (OVD) (3% Sodium Hyaluronate). FDA Summary of Safety and Effectiveness Data. 2012
14. Jabs DA, Nussenblatt RB, Rosenbaum JT; Standardization of Uveitis Nomenclature Working Group. Standardization of uveitis nomenclature for reporting clinical data. Results of the First International Workshop. *Am J Ophthalmol*. 2005;140:509–516
15. Rainer G, Menapace R, Schmid KE, Sacu S, Kiss B, Heinze G, Findl O. Natural course of intraocular pressure after cataract surgery with sodium chondroitin sulfate 4%-sodium hyaluronate 3% (Viscoat). *Ophthalmology* 2005;112:1714–1718
16. Rainer G, Menapace R, Findl O, Sacu S, Schmid K, Petternel V, Kiss B, Georgopoulos M. Effect of a fixed dorzolamide-timolol combination on intraocular pressure after small-incision cataract surgery with Viscoat. *J Cataract Refract Surg* 2003;29:1748–1752
17. Schargus M, Suckert N, Schultz T, Kakkassery V, Dick HB. Femtosecond laser-assisted cataract surgery without OVD: a prospective intraindividual comparison. *J Refract Surg* 2015;31:146–152
18. Arshinoff SA, Jafari M. New classification of ophthalmic viscosurgical devices—2005. *J Cataract Refract Surg* 2005;31:2167–2171
19. Oshika T, Okamoto F, Kaji Y, Hiraoka T, Kiuchi T, Sato M, Kawana K. Retention and removal of a new viscous dispersive ophthalmic viscosurgical device during cataract surgery in animal eyes. *Br J Ophthalmol* 2006;90: 485–487
20. Armitage WJ, Dick AD, Bourne WM. Predicting endothelial cell loss and long-term corneal graft survival. *Invest Ophthalmol Vis Sci* 2003;44: 3326–3331
21. Moschos MM, Chatziralli IP, Sergentanis TN. Viscoat versus Visthesia during phacoemulsification cataract surgery: corneal and foveal changes. *BMC Ophthalmol* 2011;11:9
22. Bourne RR, Minassian DC, Dart JK, Rosen P, Kaushal S, Wingate N. Effect of cataract surgery on the corneal endothelium: modern phacoemulsification compared with extracapsular cataract surgery. *Ophthalmology* 2004; 111:679–685

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