Original Article

Corneal Endothelial Health after Phacoemulsification Cataract Surgery without Viscoelastic Substance

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Abstract

Purpose: To evaluate corneal endothelial health after cataract surgery without viscoelastic substance (VS).

Methods: A prospective, non-randomized, case-series study was developed, and phacoemulsification cataract surgery without VS was performed on 1324 eyes between September 2015 and September 2018. As main outcomes, mean endothelial cell density (ECD) and mean central corneal thickness (CCT) were assessed before surgery and then 6 and 12 months after surgery. Data are summarized as mean, standard deviation (SD), and 95% confidence intervals (CI).

Results: A total of 1324 eyes were operated, and 31 were excluded by intraoperative complications. The mean ECD baseline was 2506 cells/mm^2 (SD = 215, CI = 2494–2518); 6 months after surgery, it was 2328 cells/mm^2 (SD = 213, CI = 2316–2340); and 1 year after surgery, it was 2265 cells/mm^2 (SD = 214, CI = 2253–2277). In terms of percentage differences, the mean ECD decrease was 9.4% after 1 year. The mean preoperative CCT was 531.6 µm (SD = 34.8, CI = 529.7–533.5); 6 months after surgery, it was 537.7 µm (SD = 38.2, CI = 535.6–539.8); and 1 year after surgery, it was 537.9 µm (SD = 37.9, CI = 535.8–540.0). The mean CCT increased 1.2% 1 year after surgery.

Conclusions: Phacoemulsification cataract surgery can be completely performed without VS, with very low intraoperative complications. The postoperative ECD and CCT changes occurred primarily during the first 6 months, and the changes decreased during the second semester.

Keywords: Cataracts, Corneal endothelial cells, Phacoemulsification, Viscoelastic substance, Viscoless

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Introduction

The cornea and the lens are the main optical structures of the eye, and both of them are affected by aging: the number of corneal endothelial cells decreases, the lens loses its transparency, and cataracts appear.[1,2] With increasing life expectancy, the demand for cataract surgery is projected to grow rapidly in upcoming years. This surgical procedure can cause endothelial cells to be damaged, and postoperative corneal decompensation after cataract surgery can occur with different degrees of severity, depending on the selected procedure, technique, and device.[3-8]

Phacoemulsification was described as a new technique for cataract removal and was published by Kelman in 1967.[9] Due to cost-effectiveness and low complication rates, it is the most widely used technique around the world. Concerns regarding corneal endothelial health during phacoemulsification are not new, and the damage seems to be directly associated with the level of ultrasound energy employed and the amount of time it lasts.[6] Nevertheless, the endothelium can also be affected during the implantation of an intraocular lens, during a corneal incision, or during the process of the anterior capsulotomy.[7,8]

In 1972, Balazs *et al.* introduced the concept that hyaluronic acid could be used as a vitreous and humor aqueous replacement.[10] In 1977, an animal experiment showed that sodium hyaluronate placed in the anterior chamber prior to pseudophakic implantation decreased postoperative corneal

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edema.[11] This idea gained attraction, and a product of sodium hyaluronate (Healon®) was commercially developed and later proved its safety and efficiency in human anterior segment surgeries.[12] More viscoelastic substances (VSs) with different properties were developed after this, and they became relevant surgical supplies that facilitated procedures in the anterior chamber, protecting the corneal endothelium.[13] However, there were also some problems, such as the postoperative rise of intraocular pressure (IOP) due to inadequate VS removal.[14,15] Anterior chamber reaction and inflammation associated with VS were also described as an anterior toxic segment syndrome.[16,17]

A new procedure was recently developed to perform phacoemulsification technique while completely avoiding the use of VS.[18] Whereas the results in terms of surgical time, costs, and potential complications are promising, a more rigorous assessment regarding corneal health outcomes is required to validate the procedure. Thus, the purpose of this work is to evaluate corneal endothelial health after phacoemulsification cataract surgery is performed without VS. In this article, we will present a brief summary of the procedure, along with the main findings obtained in clinical outcomes related to corneal health.

Methods

Study design

A prospective non-randomized case-series study was designed to evaluate phacoemulsification cataract surgery outcomes performed without VS between September 2015 and September 2018. The study was set in a private ophthalmic clinic in Buenos Aires, Argentina. The protocol and participant researchers adhered to the tenets of the Declaration of Helsinki and the approval of Dr. Nano Eye Clinic Institutional Review Board/Ethics Committee was obtained. Patients were informed about the study, and their written consent was obtained prior to participation.

Participants, inclusion, and exclusion criteria

The classification of all patients according to Lens Opacities Classification System III (LOCS III) was performed by the same surgeon (GR. B.) through slit-lamp examination. The inclusion criteria were outlined to patients with cataracts that were classified as nuclear opalescence (NO)1 – nuclear color (NC)1 to NO4–NC4 – and patients with cataract and glaucoma, only if IOP was controlled (below 21 mmHg) and stable (with lowering glaucoma drops) at least 3 months before surgery. The exclusion criteria were set to patients with cataracts classified as NO5–NC5 or worse; patients with posttraumatic cataracts; patients with a preoperative endothelial cell density (ECD) below 2000 cells/mm^2; patients with corneal pathology (herpes, corneal scar, and previous corneal refractive surgery); and patients with pseudoexfoliation, pupil synechiae or small pupil, uveitis, and/or previous vitreoretinal surgeries and/or previous glaucoma surgery. Furthermore, patients with an IOP higher than 21 mmHg were excluded, and another more appropriate surgical technique was recommended. Moreover, patients were excluded if they could not complete a 12-month follow-up. If intra-surgical complications occurred, such as posterior capsular rupture with vitreous loss, the case was excluded from the study but was registered, and the complication was analyzed and described. All the surgeries were performed by the same surgeon (GR. B.). The lens power calculation was performed with intraocular lens (IOL) Master 500 (Zeiss). One-piece hydrophilic aspheric IOLs were used in all surgeries, monofocal or multifocal, according to patient preference (SeeLens AF or SeeLens MF; HanitaLens, Israel).

Main outcomes

At baseline (1 week preoperative), all patients underwent a complete ophthalmic examination and biometry, followed by postoperative evaluations done according to the following timeline: 1 day, 1 week, 1 month, 6 months, and 12 months. Postoperative anterior chamber inflammation was evaluated, with special emphasis placed on detecting the potential presence of toxic anterior segment syndrome (TASS) or signs of endophthalmitis. The complete collected data were evaluated and processed at different time points:

1. Uncorrected distance visual acuity (UDVA) was measured during the preoperative phase and then 12 months after surgery, using a Snellen chart and converted to the logMAR
2. IOP was measured during the preoperative phase by Goldmann tonometry and then at the following postoperative time points: 1 day, 1 week, and 1 year after surgery
3. Corneal health: ECD and central corneal thickness (CCT) were measured with an endothelial specular microscope Tomey EM-4000 and its integrated software (Tomey Inc, Erlangen, Germany). Measurements were performed at baseline and 6 months and 12 months after surgery. For endothelial evaluation, the image acquisition was always performed by the same technician. Patients were asked to look at the central fixation target, and the auto-alignment function was used. The average of three consecutive measurements was registered.

Surgical technique

A detailed account of the surgical procedure is available elsewhere.[18]

1. Under topical anesthesia (0.5% proparacaine hydrochloride), two clear corneal incisions of 20 gauge (G) were performed with a disposable surgical knife (V-lance) near the limbus. The first one was at the 2 o'clock mark, and the second was at the 10 o'clock mark.
2. Immediately after the first incision, the irrigation/aspiration (I/A) bimanual handpiece 21G cannula was introduced; the second incision was then performed, and the micro-capsulorhexis forceps of 23G was introduced. The size of the tools and the incisions were selected to avoid leakage through the corneal incision and to be able to safely perform the movements
3. The irrigation bottle with a balanced salt solution (BSS) was elevated between 80 and 100 cm above the patient's

head (no more than that to avoid IOP increase), to obtain a deep and stable space in the anterior chamber. In each case, the anterior chamber was maintained with more or less BSS irrigation, which was controlled with the phacoemulsification pedal. The irrigation cannula has two lateral vents, which let the BSS leave and move in a centripetal way toward the equator

4. Capsulorhexis was performed while the liquid (BSS) circulation in the anterior chamber maintained a positive pressure, creating a stable and safe space to work
5. After that, hydrodissection was performed with the same I/A cannula until a complete rotation of the nucleus was observed
6. Then, without removing the I/A cannula, the second corneal incision was increased according to the phaco tip for the IOL implantation (2.2 mm to 2.8 mm in the present series)
7. Phacoemulsification, aspiration, and mass extractions were performed. In this study, an Infinity® equipment (Alcon) was used, with an "ozil burst" mode and the following parameters: 60 ultrasound limit; 70 on ms of burst; 300 of vacuum; and 30 aspiration rate. Vertical or horizontal "phacochop" was performed according to the cataract hardness
8. The IOL was injected, delivered, unfolded, and appropriately placed in the bag.

Finally, an intracameral antibiotic (cefuroxime) was injected, and the surgery was concluded. Postoperative topical treatment was the same in all cases: starting with gatifloxacin 0.5% and bromfenac 0.09%, 3 days before the surgery, and four times a day. Patients continued the treatment after surgery, adding one more drop, also for four times a day: difluprednate 0.05%. All the drops were maintained for a week. The treatment then changed to gatifloxacin 0.03% and dexamethasone 0.1%, 4 times a day for 3 weeks.

Statistical analysis

Descriptive statistics for all outcome variables (UDVA, IOP, ECD, and CCT) were performed. Data are summarized as mean, standard deviation (SD), and 95% confidence intervals (CI) for all time points assessed for each variable, unless stated otherwise. Furthermore, data are presented graphically using boxplots, in which the central line represents the median, the box represents the 25th and 75th percentiles, the whiskers represent the 5th and 95th percentiles, and the dots outside the whiskers represent extreme values (smaller than the 5th percentile or larger than the 95th percentile). ECD, CCT, and IOP values were analyzed using a linear mixed-effects model (LMM), with preoperative values as covariate and factors: eye (levels: left eye, right eye) and time (levels: 6 months and 12 months for ECD and CCT and 1 day, 1 month, and 1 year for IOP). The model included a random intercept and a random slope for the factor eye. Model estimates and their corresponding CI are reported, as well as marginal and conditional R^2 values.[19] The computation of P values is based on conditional F-tests with Kenward–Roger approximation for the degrees of freedom.

Results

A total of 1324 eyes were operated in this study. Twenty-three eyes (1.73%) were excluded due to the following intra-surgical complications: flat anterior chamber during surgery (11 cases), anterior capsular rupture (10 cases), and partial zonular rupture (2 cases). All complications were resolved during the same surgery. For those cases, VS was used, and postoperative evolution was good. The rest of the 1301 uncomplicated operated eyes from 651 patients were evaluated. The mean age was 71.78 ± 7.37 years old, from 354 (54.37%) women and 297 (45.63%) men. TASS and endophthalmitis did not occur in any of these cases.

Figure 1 shows the distribution of UDVA values measured at two time points: preoperative and 1 year after surgery. The mean preoperative UDVA was 0.55 logMAR (SD = 0.25, CI = 0.53–0.57); 1 year post-surgery, the mean UDVA was 0.04 (SD = 0.05, CI = 0.03–0.05).

Figure 2 shows the distribution of IOP measured before surgery, and at three different postoperative time points. The mean preoperative IOP was 14.0 mmHg (SD = 1.8, CI = 13.9–14.1). One day after surgery, the mean IOP was 13.9 mmHg (SD = 1.8, CI = 13.8–14.0); 1 month after surgery, the mean IOP was 14.0 mmHg (SD = 1.6, CI = 13.9-14.1); and finally, 1 year after surgery, the mean IOP was 14.1 mmHg (SD = 1.7, CI = 14.0–14.2). Table 1 shows the LMM analysis for IOP. The results show that preoperative values are a statistically significant predictor of IOP ($P < 0.001$), and there are statistically significant differences of IOP at each assessed time ($P < 0.001$).

Figures 3 and 4 show the distribution of ECD and CCT, respectively, measured before surgery and at two different postoperative time points. The mean preoperative ECD was 2506 cells/mm^2 (SD = 215, CI = 2494–2518); 6 months after surgery, the mean ECD was 2328 cells/mm^2 (SD = 213, CI = 2316–

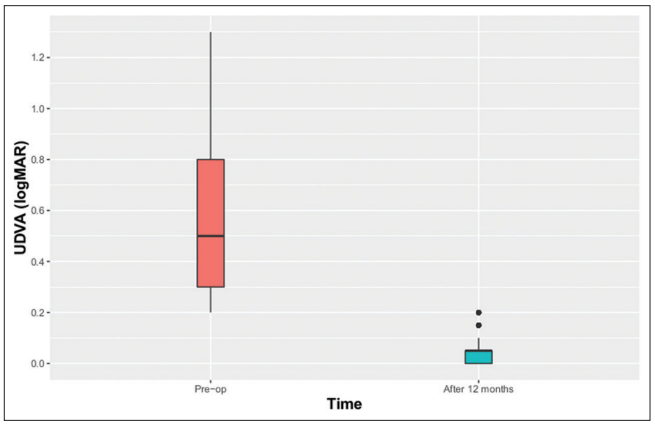

Figure 1: The uncorrected distance visual acuity values measured preoperative and 1 year after surgery

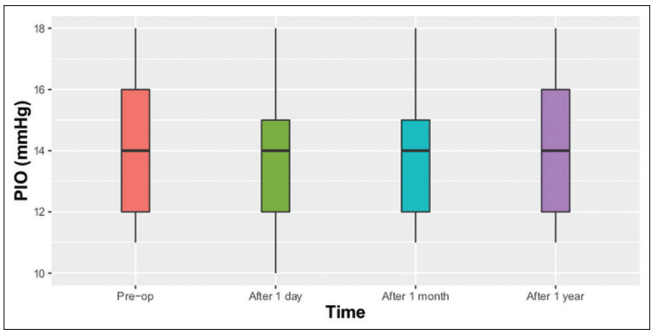

Figure 2: The distribution of intraocular pressure, before surgery and at three different postoperative time points

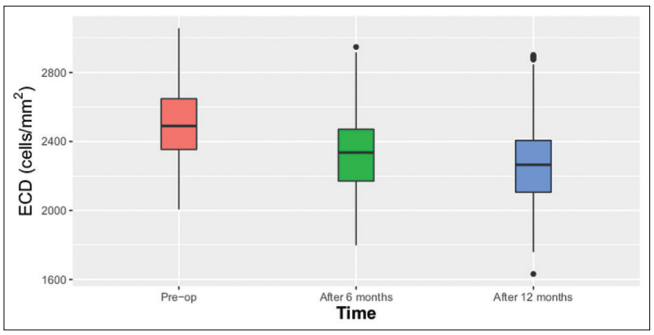

Figure 3: The mean endothelial cell density distribution evaluated before surgery and at 6 months and 1 year after surgery

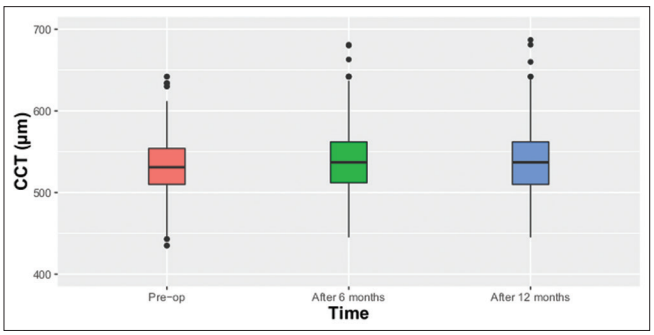

Figure 4: The mean central corneal thickness is shown at different postoperative time points

2340), whereas a year after surgery, the mean ECD was 2265 cells/mm^2 (SD = 214, CI = 2253–2277). In terms of percentage differences, the mean ECD decrease was 6.9% (SD = 6.4, CI = 6.6–7.2) after 6 months, and 9.4% (SD = 6.7, CI = 9.0–9.8) after a year. With regard to CCT, the mean preoperative CCT was 531.6 µm (SD = 34.8, CI = 529.7–533.5); 6 months after surgery, the mean CCT was 537.7 µm (SD = 38.2, CI = 535.6–539.8); and a year after surgery, the mean CCT was 537.9 µm (SD = 37.9, CI = 535.8–540.0). In terms of percentage differences, the mean CCT increased 1.1% (SD = 3.4, CI = 0.9–1.3) 6 months after surgery and 1.2% (SD = 3.4, CI = 1.0–1.4) 1 year after surgery.

LMM analyses for ECD and CCT are shown in Tables 2 and 3, respectively. It can be observed that preoperative values are again significant predictors for both variables ($P < 0.001$), but there were statistically significant differences in time only for ECD ($P < 0.001$).

Table 1: Linear mixed effects model analysis for intraocular pressure

	IOP		
Predictors	**Estimates**	**CI**	***P***
Intercept	7.26	6.60-7.92	<0.001
Preoperative IOP	0.46	0.42-0.50	<0.001
Eye	0.03	−0.11-0.17	0.695
Time	0.12	−0.10-0.14	<0.001
N subject ID	651		
Observations	3903		
Marginal R^2/conditional R^2	0.233/0.903		

Effect estimates, confidence intervals, and *P* values are reported for the fixed effects (eye, time) and the covariate (preoperative IOP), along with the marginal and conditional R^2. IOP: Intraocular pressure, CI: Confidence interval

Table 2: Linear mixed-effects model analysis for endothelial cell density

	ECD		
Predictors	**Estimates**	**CI**	***P***
Intercept	757.62	655.60-859.64	<0.001
Preoperative ECD	0.66	0.62-0.70	<0.001
Eye	−6.30	−21.43-8.72	0.410
Time	−62.97	−67.09-−58.85	<0.001
N subject ID	651		
Observations	2602		
Marginal R^2/conditional R^2	0.453/0.938		

Effect estimates, confidence intervals, and *P* values are reported for the fixed effects (eye, time) and the covariate (preoperative ECD), along with the marginal and conditional R^2. ECD: Endothelial cell density, CI: Confidence interval

Table 3: Linear mixed-effects model analysis for central corneal thickness

	CCT		
Predictors	**Estimates**	**CI**	***P***
Intercept	26.33	11.42-41.24	0.001
Preoperative CCT	0.96	0.93-0.99	<0.001
Eye	−0.25	−2.16-1.66	0.794
Time	0.19	−0.14-0.52	0.258
N subject ID	651		
Observations	2602		
Marginal R^2/conditional R^2	0.776/0.987		

Effect estimates, confidence intervals, and *P* values are reported for the fixed effects (eye, time) and the covariate (preoperative CCT), along with the marginal and conditional R^2. CCT: Central corneal thickness, CI: Confidence interval

Discussion

This article evaluates outcomes following cataract surgeries performed with a technique that completely avoids the use

of VS. Visual acuity was improved as expected, and IOP remained stable a year after surgery. Nevertheless, the main concern was focused on two postoperative corneal health parameters (ECD and CCT). Their changes occurred 1 year after surgery, and their clinical relevance will be discussed. The potential advantage of performing this surgical technique without VS will also be described.

There are several studies that describe problems related to VS. For example, VS induces an increase in IOP through a reduction of aqueous outflow due to blockage of the trabecular meshwork where the fluids exit the eye.[13,14] Therefore, complete removal of VS is necessary to avoid an IOP rise, which can be more relevant in glaucoma patients with previous optic nerve damage.[20] Furthermore, "flare or tyndall effect" can be postoperatively detected, which could be the manifestation of TASS after cataract surgery, and VS could be associated with this.[16,17] Also, a longer surgical time is required in order to introduce, and later remove VS from the anterior chamber. Whereas VS helps in performing safer surgeries, it can also be the cause of other problems that can sometimes be serious.

Due to that, there are some studies describing how VS can be partially or completely avoided. Schulze *et al*. avoided the use of VS only during IOL implantation, without finding differences in endothelial cell loss.[21] Oksuz *et al*. described a technique to perform capsulorhexis without VS, but they were used after hydrodissection, and for the IOL implantation.[22] Wright *et al*. compared their results of small-incision extracapsular cataract surgery using the anterior chamber maintainer without VS, and they finally showed that the magnitude and range of the endothelial cell loss associated with this technique were significantly greater than those described following phacoemulsification.[23] Due to this, these authors finally recommend the use of VS for this extracapsular procedure. However in 2008, Sallet described a phacoemulsification cataract surgery technique completely performed without VS where he found no difference in clinical outcomes in a comparison done with 50 patients operated with VS.[24]

The technique described in this work proposes two corneal microincisions (20G V-lance) and the enlargement of one of those to 2.2–2.8 mm, according to the phacoemulsification tip (Sallet open 2.6 mm). Another difference with the technique described by Sallet is about hydrodissection. in the present technique, it is performed by a 23G I/A cannula. Positive preliminary results in clinical outcomes using this technique led to this study, in which the goal was to evaluate clinical outcomes of cataract surgery without VS in a large sample. In particular, ECD and CCT were assessed as main outcomes. It is presumed that when ECD decreases under a critical number, the cornea swells, causing CCT to increase, resulting in affected or lost transparency.[2,3,25,26] Furthermore, there are many different factors which could affect ECD during phacoemulsification cataract surgery, such as the characteristics of the phacoemulsification device, the total surgery time and the energy delivery, phaco-mode, and last but not least, the surgeon's experience.[3-8] A prospective study performed by Kugu *et al*.,[27] comparing two groups of patients operated with and without VS, was published in 2015. They could not determine a protective effect of 1.0% sodium hyaluronate over BSS on ECD loss during phacoemulsification. Another work comparing femtosecond laser-assisted cataract surgery performed without VS versus standard phacoemulsification with VS was published in the same year. They could not find any significant statistical difference of ECD loss between groups 6 months after surgery.[28]

It is well known that endothelial corneal cells decrease after cataract surgery. Nevertheless, there is a great variability in literature regarding the percentage of loss after phacoemulsification, ranging from 3.1%[27] to 18.46%.[28] In this study, ECD decreased 7.11% in the first 6 months following surgery and 2.51% more in the second postoperative semester, completing a total decrease of 9.62% 1 year after surgery. It will be interesting to evaluate what happens 2 years after surgery since the present group of patients will still be under follow-up. Another piece of information to point out is the 1.13% CCT increase in the first 6 months and the 0.03% increase in the 6 months after that (total increase after 1 year was 1.16%). This information suggests that the cornea does not suffer any more changes after the "first postoperative 6 months". However, as can be seen in Figures 3 and 4, there are some outlier cases. It is necessary to study another preoperative and intraoperative parameters (as example: age, cataract grade, phacoemulsification time, and intraocular energy delivered) to understand what happens in those outlier cases and improve the indications of this surgical technique. Future studies can provide more information regarding that.

The results of this study show that the ECD loss and the CCT increase after an 1-year follow-up were similar to previously published studies, in which surgery was performed with VS.[29,30] Moreover, the IOP remains stable throughout the complete follow-up time, and none of the eyes developed a postoperative IOP rise. Accordingly, in the LMM analysis, those parameters remained stable over time. Statistically significant differences observed for these parameters are due to the large sample size, but it is clear from the plots and the descriptive statistics that differences over time are not clinically relevant at 1 year of follow-up. Furthermore, no statistical or clinical differences were observed between left or right eyes. In this study, with a 1-year follow-up, the principal strength lies in the large number of cases (1301 eyes). Undoubtedly, a comparative case series study (phaco with VS vs. without VS) will be necessary to confirm these results. Meanwhile, it was recently used in another study performed to evaluate spectacle independence after cataract surgery, implanting multifocal lens, further emphasizing confidence in this surgical technique.[31] Regarding the ECD and CCT parameters, similar results were obtained in 480 eyes 1 year after surgery.

In regard to the advantages of this proposed technique, we can point to the fact that VS-related complications such as IOP postoperative rise, occasional TASS occurrence,

and endothelial corneal damage during VS aspiration were completely avoided. Furthermore, surgery time is reduced since it is not required to inject and extract VS from the anterior chamber. Finally, the surgery is performed with positive pressure in the anterior chamber at all times; this allows the capsulorhexis to be easily performed. Possibly, this technique may not be recommended for recently graduated surgeons and in regard to limitations or contraindications, this technique is not recommended for patients with endothelial corneal pathology, pseudoexfoliation syndrome, traumatic cataracts, and/or a history of previous vitreoretinal surgery; patients with "hard" cataracts; or those who have been prescribed with three-piece IOLs or patients with endothelial corneal pathology. Furthermore, if there are complications during capsulorhexis, the surgery should revert to a standard procedure including VS. As a final recommendation, ECD should be a mandatory preoperative study, and a minimum six months of follow-up time is recommended after surgery. In addition to this, hydrodissection must be performed without pressing over the posterior capsule to avoid rupture. Moreover, the IOL implantation should be performed in a well-expanded anterior chamber.

In summary, this present work shows that phacoemulsification cataract surgery can be completely performed without VS, with very low intraoperative complications. Corneal health remained stable 1 year after surgery. The postoperative ECD and CCT changes occurred principally during the first 6 months and decreased during the second semester. Visual acuity achieved was good in all the study groups, and there were no changes in IOP during the 1-year follow-up.

This surgical technique seems to be secure for the cornea, or, at least, similar to standard procedures in which VS is used but with potential advantages that were pointed out in the discussion of this work. These results must be reconfirmed by the experiences of other surgeons in a prospective multicentric randomized clinical study. Meanwhile, the standard procedure of using viscoelastic should be followed.

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Conflicts of interest

There are no conflicts of interest.

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