# Natural Course of Intraocular Pressure after Cataract Surgery with Sodium Chondroitin Sulfate 4%–Sodium Hyaluronate 3% (Viscoat)

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***Purpose:*** To investigate the natural course of intraocular pressure (IOP) and its peak after small-incision cataract surgery with chondroitin sulfate 4%–sodium hyaluronate 3% (Viscoat, Alcon Laboratories, Inc., Fort Worth, TX).

***Design:*** Observational case series.

***Participants:*** This prospective study comprised 40 eyes of 40 consecutive cataract patients scheduled for small-incision cataract surgery.

***Methods:*** Cataract surgery was performed with sodium chondroitin sulfate 4%–sodium hyaluronate 3% as the ophthalmic viscosurgical device, which was removed as completely as possible from the eye at the end of surgery. The IOP was measured preoperatively and 30 minutes; 1, 2, 3, 4, 6, 8, and 20 to 24 hours; and 1 week postoperatively.

***Main Outcome Measures:*** Postoperative IOP increase.

***Results:*** The mean IOP increased significantly at all observation times during the first 20 to 24 hours, with a peak increase of 13.4±9.4 mmHg after 1 hour ($P<0.05$). In all, 28 eyes (70%) had an IOP spike to 30 mmHg or higher. Sixty-eight percent of these spikes occurred at 30 minutes as well as at 1 hour and 2 hours postoperatively. At 20 to 24 hours, no eye had an IOP spike to 30 mmHg or higher.

***Conclusions:*** Significant IOP increases were found during the first 24 hours, peaking at 1 hour after surgery. With a single postoperative IOP measurement, between 30 minutes and 2 hours after surgery, two thirds of these IOP spikes could be detected. To detect all IOP spikes, a second measurement between 4 and 6 hours after surgery would be necessary. *Ophthalmology 2005;112:1714–1718 © 2005 by the American Academy of Ophthalmology.*

An increase in intraocular pressure (IOP) is the most frequent complication in the early postoperative period after cataract surgery.[1] This has become a major concern as an increasing number of cataract patients are having surgery in an outpatient setting and are discharged soon after surgery.

The use of an ophthalmic viscosurgical device (OVD) and implantation of a foldable intraocular lens (IOL) is currently the standard technique in cataract surgery.[2] Despite their advantages, OVDs have the disadvantage of sometimes causing high increases in IOP within the first 24 hours postoperatively.

In several studies, an increase in IOP after small-incision cataract surgery has been reported.[3–10] However, in all studies, IOP was measured only once or twice in the early postoperative period. Thus, the exact course of IOP increase after cataract surgery and the time of its peak remain unknown. It is also of interest to determine the best postoperative time point for measuring IOP for the purpose of detecting IOP spikes with highest sensitivity.

We therefore conducted a prospective study to evaluate the natural course of IOP and its peak after small-incision cataract surgery with sodium sulfate 4%–sodium hyaluronate 3% (Viscoat, Alcon Laboratories, Inc., Fort Worth, TX), which is to date the most frequently used OVD in the United States among members of the American Society of Cataract and Refractive Surgery (ASCRS).[2]

## Patients and Methods

This prospective study comprised 40 eyes of 40 consecutive cataract patients scheduled for small-incision cataract surgery and

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implantation of a foldable IOL. The study protocol was approved by the ethics committee of the Vienna University School of Medicine. Written informed consent was obtained from all patients included. Exclusion criteria were previous ocular surgery, glaucoma or ocular hypertension (IOP > 22 mmHg). Thirty-two of the patients were women, and 8 were men. The mean patient age was 76.7±9.2 years.

All patients were operated by the same surgeon (RM). Approximately 1 to 2 hours before surgery, diclofenac, phenylephrine 2.5%, tropicamide 0.5%, and cyclopentolate 1% eyedrops were instilled. After peribulbar anesthesia, a temporal single-plane 3.2-mm posterior limbal incision was performed. Sodium chondroitin sulfate 4%–sodium hyaluronate 3% was used as the OVD. Capsulorrhexis, hydrodissection, and phacoemulsification of the nucleus were followed by aspiration of the cortical remnants and cleaning of the capsular bag. The capsular bag was then expanded with the OVD, and a foldable 3-piece IOL was implanted into the capsular bag. The OVD was aspirated in a standardized fashion from the retrolental space, the capsule fornix, and the anterior chamber using an I/A tip. First, the proximal optic edge was tilted up with a spatula and the I/A tip inserted behind the optic. After the central portion of the OVD was removed, the I/A tip was swept across and along the capsular equator to capture peripheral residuals. The irrigation/aspiration (I/A) tip was then guided into the anterior chamber and the optic repositioned. While the aspiration opening was rotated right, left, and posteriorely, the OVD was removed circumferentially from the prelental, retroiridal, and preiridal spaces. The surgeon was careful not to approach the delicate structures of the endothelium and the chamber angle too closely. Consequently, the residual film coating these structures often was observed to persist. Finally, the I/A tip was positioned on the center of the optic; while the aspiration opening was directed upwards and the tip pressed down on the optic, the anterior chamber was rinsed before retraction of the I/A tip. The incision was left sutureless. No miotic agent was used intracamerally. At the end of surgery, the IOP was measured by Schiøtz tonometry and adjusted to 20 mmHg. Capsular rupture did not occur in any patient. After surgery, the eye was patched with prednisolone acetate 0.5% ointment. No antiglaucoma medication was administered. After the 20- to 24-hour visit, diclofenac and prednisolone acetate 0.5% eyedrops were used 4 times a day.

The baseline IOP was measured by Goldmann applanation tonometry 1 day before surgery. The IOP was measured with the same Goldmann applanation tonometer 30 minutes and 1, 2, 3, 4, 6, 8, and 20 to 24 hours after surgery. At each observation time, the IOP was measured twice. If the IOP measurement differed by ≥2 mmHg, a third measurement was performed and the median was taken for statistical analysis. If the IOP reached ≥50 mmHg (2 eyes, at 1 and at 3 hours after surgery, respectively), eyes were treated with local and systemic antiglaucoma medication and IOP measurements after medication were excluded from statistical analysis. A routine follow-up including IOP measurement was performed 1 week after surgery.

### Statistical Analysis

Repeated-measures analysis of variance was used to reveal differences between postoperative and preoperative IOP measurements. The compound symmetry covariance structure was specified, allowing the variance to be different at various time points. Comparisons of postoperative IOP measurements with the baseline measurement were adjusted for multiple comparisons using the Dunnett–Hsu post hoc test. The software SAS/Proc Mixed version 9.1 (SAS Institute Inc., Cary, NC) was used for statistical analysis. $P$ values of $<0.05$ were considered as indicating statistical significance.

## Results

Mean preoperative and postoperative IOP values are depicted in Figure 1. The mean preoperative IOP was 15.4±2.7 mmHg, climbed to 27.1±8.7 at 30 minutes postoperatively, reached its peak at 1 hour postoperatively with 28.8±8.9, and then slowly declined to 28.6±7.6, 27.5±8.3, 26.3±7.0, 24.8±6.6, and 22.5±5.7 at 2, 3, 4, 6, and 8 hours after surgery, respectively. Mean IOP was 17.0±3.9 mmHg at 20 to 24 hours and 15.5±4.5 at 1 week after surgery. At 20 to 24 hours, no eye had an IOP spike of ≥30 mmHg. At 1 week after surgery, 1 eye had an IOP of 32 mmHg. In that eye we discontinued therapy with prednisolone acetate eyedrops, and IOP decreased to its preoperative value at 2 weeks after surgery.

Table 1 shows the mean IOP changes from before the operation. Mean IOP increases relative to preoperatively were 11.8±9.2 mmHg, 13.4±9.4 (peak), 13.2±7.2, 12.1±7.9, 11.0±7.0, 9.6±6.4, and 6.8±5.4 at 30 minutes and 1, 2, 3, 4, 6, and 8 hours after surgery, respectively. These increases were significant at each observation time ($P<0.001$). At 20 to 24 hours after surgery, the mean increase was 1.8±3.0 ($P = 0.031$). At 1 week after surgery, IOP reached preoperative values ($P = 1.0$).

The maximum IOP value of each eye was found in 12 eyes at 1 hour, followed by 9, 8, and 5 eyes at 30 minutes and 2 and 3 hours after surgery, respectively. Only 6 eyes had their maximum IOP value later than 3 hours after surgery. The highest IOP values were 52 and 50 mmHg, detected at 1 and 3 hours after surgery, respectively. Both eyes were treated with local and systemic antiglaucoma medication. All other IOP values were <50 mmHg and were not treated.

Table 2 shows the number and percentage of eyes with a postoperative IOP spike to ≥30 mmHg. In all, IOP spikes to ≥30 occurred in 28 eyes (70%). The most frequent IOP spikes occurred at 30 minutes, as well as at 1 and 2 hours after surgery (19 IOP spikes each), followed by 17, 12, 10, and 3 IOP spikes at 3, 4, 6, and 8 hours after surgery, respectively. Table 2 also shows the percentage of IOP spikes detected by a single postoperative measurement. A single IOP measurement at 30 minutes and 1 or 2 hours after surgery could detect 68% of IOP spikes; at 3 hours, 61%; and at 6 hours, only 36%. For detection of all eyes with an IOP spike to ≥30, 2 IOP measurements—the first, 30 minutes to 2 hours postoperatively, and the second, between 4 and 6 hours postoperatively—would be necessary.

## Discussion

This study demonstrates that sodium chondroitin sulfate 4%–sodium hyaluronate 3% causes significant IOP increases in the early postoperative period, with a peak at 1 hour postoperatively.

Sodium chondroitin sulfate 4%–sodium hyaluronate 3% is a dispersive OVD with low viscosity at zero shear rate. The dispersive nature causes better adherence of the OVD to the corneal endothelium,[11] possibly resulting in better protection of the corneal endothelium against fluid turbulence and lens fragments during phacoemulsification. This has led to frequent use of dispersive OVDs in routine small-incision cataract surgery. In the U.S., among members of the ASCRS a survey showed that sodium chondroitin sulfate 4%–sodium hyaluronate 3% is the most frequently used OVD during cataract surgery.[2] In combination with sodium hyaluronate 1% (ProVisc, Alcon Laboratories) in 1 packet (DuoVisc, Alcon Laboratories), it was used by

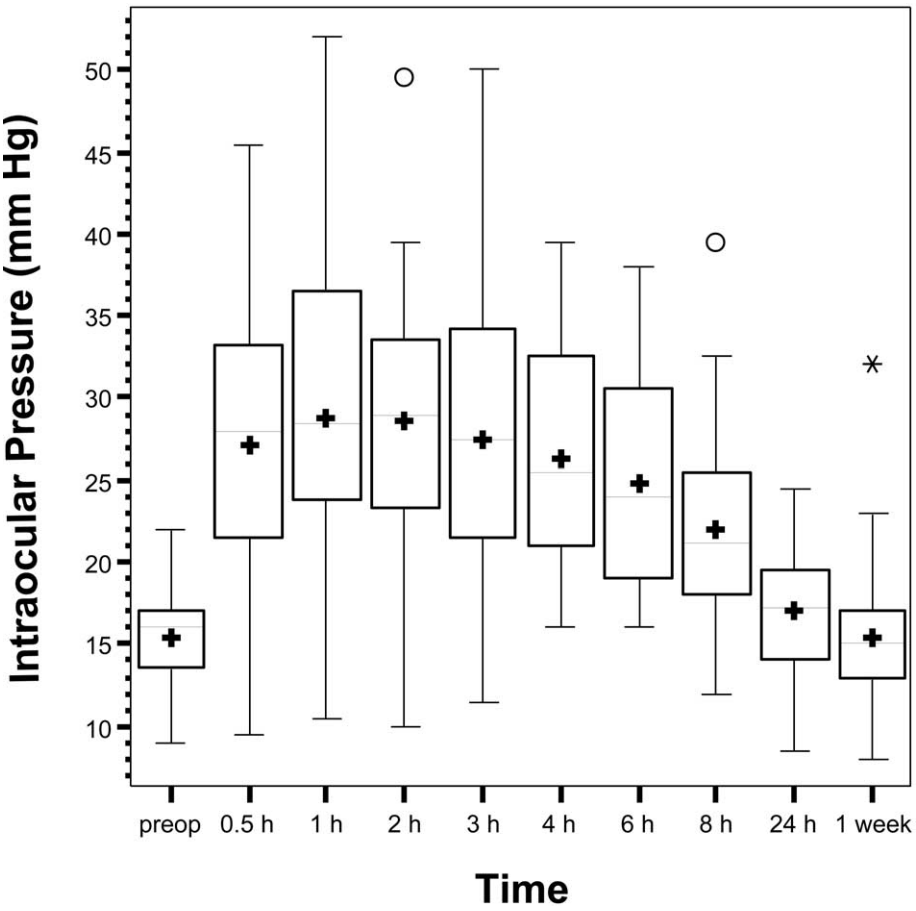


**Figure 1.** Mean preoperative (preop) and postoperative intraocular pressure (IOP). h = hours. +, mean IOP; ○, outlier (>1.5 times the interquartile range above the 75th percentile). *Extreme outlier (>3 times the interquartile ranges above the 75th percentile).

37% of respondents, followed by sodium chondroitin sulfate 4%–sodium hyaluronate 3% alone (16%), sodium hyaluronate 1.6% (Amvisc Plus, Bausch & Lomb, Rochester, NY) (7%), sodium hyaluronate 1% (Healon, Advanced Medical Optics, Uppsala, Sweden) (6%), sodium hyaluronate 1.4% (Healon GV, Advanced Medical Optics) (5%), sodium hyaluronate 1% (ProVisc) (6%), sodium hyaluronate 1% (Amvisc, Bausch & Lomb) (7%), sodium hyaluronate 2.3% (Healon5, Advanced Medical Optics) (3%), and hydroxypropyl methylcellulose 2% (Cellugel, Alcon Laboratories) (2%). A potential drawback of the dispersive sodium chondroitin sulfate 4%–sodium hyaluronate 3%, however, is the difficulty of completely removing it at the end of surgery, possibly resulting in an increased postoperative IOP.

Table 1. Mean Intraocular Pressure (IOP) Change (mmHg), Standard Deviation, and Range from Preoperatively to 30 Minutes; 1, 2, 3, 4, 6, 8, and 20 to 24 Hours; and 1 Week Postoperatively

| Postoperative Time | IOP Change | *P* Value |
|---|---|---|
| 30 min | 11.8±9.2 (−9 to 34) | <0.001 |
| 1 hr | 13.4±9.4 (−8 to 40) | <0.001 |
| 2 hrs | 13.2±7.2 (−6 to 28) | <0.001 |
| 3 hrs | 12.1±7.9 (−5 to 28) | <0.001 |
| 4 hrs | 11.0±7.0 (0–26) | <0.001 |
| 6 hrs | 9.6±6.4 (1–25) | <0.001 |
| 8 hrs | 6.8±5.4 (−2 to 23) | <0.001 |
| 20–24 hrs | 1.8±3.0 (−5 to 8) | 0.031 |
| 1 wk | 0.2±4.4 (−9 to 14) | 1.0 |

Table 2. Number and Percentage of Eyes with Postoperative Intraocular Pressure (IOP) Spikes to ≥30 mmHg, and Percentage of IOP Spikes Detected by a Single Postoperative IOP Measurement

| Postoperative Time | No. of Eyes | No. (%) of Eyes with IOP ≥30 mmHg | % of IOP Spikes Detected with a Single IOP Measurement |
|---|---|---|---|
| 30 min | 40 | 19 (48) | 68 |
| 1 hr | 40 | 19 (48) | 68 |
| 2 hrs | 39 | 19 (49) | 68 |
| 3 hrs | 39 | 17 (44) | 61 |
| 4 hrs | 38 | 12 (32) | 43 |
| 6 hrs | 38 | 10 (26) | 36 |
| 8 hrs | 38 | 3 (8) | 11 |
| 20–24 hrs | 38 | 0 (0) | 0 |
| Any time | 40 | 28 (70) | NA |

NA = not applicable.

The major reason for the postoperative IOP increase seems to be the amount of the remaining OVD at the end of surgery. It is assumed that the remaining viscoelastic agent mechanically obstructs the trabecular outflow pathway and, hence, decreases the outflow facility.[12] To avoid a postoperative IOP increase, a thorough removal of the OVD is vital. In our study, sodium chondroitin sulfate 4%–sodium hyaluronate 3% was removed with great care from the anterior chamber as well as from behind the IOL at the end of the surgery. However, it was nearly impossible to remove the dispersive sodium chondroitin sulfate 4%–sodium hyaluronate 3% completely without injuring the endothelium and other vulnerable structures of the eye.

In previous studies,[5,7,8] in which cataract surgery was performed by the same surgeon (RM), with the same surgical technique, we could show that sodium chondroitin sulfate 4%–sodium hyaluronate 3% caused IOP increases of 10.1, 8.6, and 8.4 mmHg, respectively, at 6 hours postoperatively. These results are comparable to the result of the present study, at which the mean postoperative IOP increase was 9.6 mmHg at 6 hours after surgery. Furthermore, we showed in previous studies[5,7,13] that, relative to chondroitin sulfate 4%–sodium hyaluronate 3%, hydroxypropyl methylcellulose 2% (Ocucoat, Bausch & Lomb), sodium hyaluronate 1% (Healon), and sodium hyaluronate 2.3% (Healon5) caused significantly lower IOP increases at 6 hours after surgery: 4.6, 4.8, and 5.2 mmHg, respectively.

However, it remains unclear at what time the maximum IOP increase occurs with the different OVDs. To date, it is widely assumed that the peak of the postoperative IOP increase is 4 to 7 hours after surgery.[14] This is contrary to the results of our present study, in which, for sodium chondroitin sulfate 4%–sodium hyaluronate 3%, the peak of the postoperative IOP increase was found at 1 hour after surgery. However, the present study is the first presenting the exact course of postoperative IOP with chondroitin sulfate 4%–sodium hyaluronate 3%. The exact courses of postoperative IOP of other OVDs remain to be investigated.

In the present study, 70% of eyes had IOP spikes to ≥30 mmHg. Sixty-eight percent of these spikes occurred at 30 minutes and 1 and 2 hours postoperatively. Fortunately, no IOP spike occurred at 20 to 24 hours postoperatively. Intraocular pressure spikes to ≥30 mmHg may be associated with corneal epithelial edema and pain and may increase the risk of retinal artery occlusion and anterior ischemic optic neuropathy.[15] Furthermore, in patients with glaucoma, IOP spikes could lead to deterioration of glaucomatous optic discs, resulting in worsening of visual fields.[16] Intraocular pressure monitoring and administration of antiglaucoma medication, especially in patients with compromised optical discs, are mandatory.

For detection of patients with an IOP spike to ≥30 mmHg, a single postoperative IOP measurement is not sufficient to detect all spikes. With a single IOP measurement between 30 minutes and 2 hours postoperatively, two thirds of spikes would be detected. A single IOP measurement at 6 hours postoperatively would detect only 36% of IOP spikes. For detection of all eyes with an IOP spike to ≥30 mmHg, 2 IOP measurements, the first between 30 minutes and 2 hours and the second between 4 and 6 hours postoperatively, would be necessary.

To date, many surgeons use antiglaucoma medication to prevent IOP spikes; however, no medication has been entirely satisfactory. In previous studies,[13,17,18] we demonstrated that, with the use of sodium hyaluronate 1%, neither brimonidine (Alphagan, Allergan Inc., Irvine, CA), apraclonidine (Iopidine, Alcon Laboratories), latanoprost (Xalatan, Pharmacia & Upjohn Co., Kalamazoo, MI), nor dorzolamide (Trusopt, Merck & Co., Inc., Whitehouse Station, NJ) prevented postoperative IOP increases. Only the fixed dorzolamide–timolol combination (Cosopt, Merck) was highly effective in preventing IOP increases and IOP spikes to ≥30 mmHg.[19] However, when sodium chondroitin sulfate 4%–sodium hyaluronate 3% was used as the OVD, the fixed dorzolamide–timolol combination could not prevent IOP increases and IOP spikes.[8] In the present study, we attempted to evaluate the exact natural course of IOP after cataract surgery. Therefore, we did not use any antiglaucoma medication.

In conclusion, our study shows that sodium chondroitin sulfate 4%–sodium hyaluronate 3% caused significant IOP increases during the first 24 hours, with a peak at 1 hour after surgery. Two thirds of eyes had an IOP spike to ≥30 mmHg. With a single postoperative IOP measurement, between 30 minutes and 2 hours after surgery, two thirds of these IOP spikes could be detected.

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