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Case Report

Evaluation of a Novel Blue-Colored Ophthalmic Viscoelastic Device Applied during Phacoemulsification in Eyes with Pseudoexfoliation Syndrome

Andreas F. Borkenstein Eva-Maria Borkenstein

Borkenstein & Borkenstein, Private Practice at Privatklinik der Kreuzschwestern Graz, Graz, Austria

Keywords

Colored ophthalmic viscoelastic device · Cataract surgery · Pseudoexfoliation syndrome · Surgical workflow · Malyugin ring

Abstract

Recently, a new development in the field of ophthalmic viscoelastic devices (OVDs) has been introduced. The blue-colored OVD Pe-Ha-Blue® PLUS combines the viscoelastic properties of OVD together with trypan blue for better visualization during surgery. The objective of this case series is to investigate whether the use of a blue-colored OVD during cataract surgery in patients with pseudoexfoliation syndrome (PXF) and narrow pupils (miosis) has advantages over the use of a clear standard OVD in combination with trypan blue. We included 52 eyes of 52 consecutive cataract patients diagnosed with PXF. Study participants were divided into two groups of 26 patients each, depending on which OVD was used during surgery (group A: blue-colored OVD; group B: standard clear OVD). Intraoperatively, we evaluated the operation time (surgery start to the beginning of phacoemulsification) and the surgeon's satisfaction with the

surgical workflow. Postoperative examinations were performed 6 h, 20 h, and 4 weeks after surgery and included corrected distance visual acuity (CDVA) and intraocular pressure (IOP). Our results show that there was a statistically significant time gain in group A in terms of surgery time. In addition, findings on surgeon satisfaction, postoperative CDVA and IOP suggest further benefits in group A. We discuss further properties and possible advantages which may result from the use of a blue-colored OVD. In summary, a blue-colored viscoelastic device can be a helpful alternative to clear OVD especially in challenging cases to improve the surgical workflow and make the whole procedure even safer and faster.

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Introduction

Ophthalmic viscoelastic devices (OVDs) are fundamental tools in modern intraocular procedures and routinely used in cataract surgery to protect delicate ocular structures, maintain the relationships of ocular structures, create space, improve visualization, pressurize the anterior chamber, and provide a faster and safer surgery with better visual recovery for the patients. Among the various viscoelastic substances, sodium hyaluronate became the most popular biopolymer used in OVD for intraocular surgery after the introduction of Healon® in 1979. Since then, extensive reviews have been published describing pharmacological, physiological, and clinical aspects of sodium hyaluronate in ophthalmological applications [1, 2]. Sodium hyaluronate (hyaluronic acid or hyaluronan) is a naturally occurring, high-molecular polysaccharide found in the extracellular matrix of connective tissues. It also occurs in the aqueous humor and the vitreous and covers the corneal endothelium.

Recently, Albomed® introduced their latest innovation in the field of sodium hyaluronate OVDs named Pe-Ha-Blue® PLUS (Albomed® GmbH, Schwarzenbruck, Germany), which combines the viscoelastic properties of Pe-Ha-Luron® F (Albomed®) with trypan blue (Fig. 1). Pe-Ha-Blue® PLUS is CE certified and available in a prefilled syringe to allow for the simultaneous administration of viscoelastic and the staining agent trypan blue in one single step.

Dr. Jean-Pierre Corlay (France) provided the basic concept behind the development of Pe-Ha-Blue® PLUS. He has performed many surgeries with mature cataracts in developing countries where the transparent capsule was indistinguishable from the opaque crystalline lens, increasing the risk of capsule rupture and other surgical complications. The use of Pe-Ha-Blue® PLUS maintains the anterior chamber of the eye and simultaneously stains the capsule to improve the overall visualization and the visibility of the capsulorhexis edge during continuous curvilinear capsulorhexis (CCC) and surgery. This should facilitate the first phase of the operation, save time, and accelerate surgical procedures to make ophthalmic interventions safer, easier, and faster. Using Pe-Ha-Blue® PLUS can therefore be particularly helpful in difficult and challenging cases and eyes with small pupils (miosis), e.g. in pseudoexfoliation syndrome (PXF), glaucoma, uveitis or synechiae, in which iris hooks or Malyugin rings are needed for mechanical pupil dilation.

The objective of this case series was to investigate whether there is a time gain from using Pe-Ha-Blue® PLUS during cataract surgery in patients with PXF and narrow pupils compared to using a clear standard OVD combined with vision blue/blue color caps to stain the anterior

capsule. Additionally, we compared the surgeon's satisfaction with the surgical workflow, visual acuity, and intraocular pressure (IOP) between both study groups.

Case Series

In this case series, we included 52 eyes of 52 consecutive patients diagnosed with senile cataract and PXF. The study adhered to the tenets of the Declaration of Helsinki and all patients signed the informed consent. All patients underwent phacoemulsification and implantation of an intraocular lens (IOL) by the same surgeon (A.F.B.). In all cases, the 6.25-mm Malyugin ring was inserted through the main incision to provide sufficient pupil dilation. The study participants were divided into two groups of 26 patients each, depending on which OVD was used intraoperatively. In group A, a novel blue-colored OVD was used (Pe-Ha-Blue® PLUS; see Fig. 1). In group B, we applied a standard clear OVD (POLYHYL® 1.6%; Polytech Domilens GmbH, Germany; see Fig. 1). The time from the start of the operation to the beginning of the phacoemulsification was measured intraoperatively using a stopwatch. Immediately after surgery, the surgeon and the scrub nurse completed a short questionnaire to evaluate their satisfaction with the surgical workflow and the OVD used. The questionnaire consisted of these 5 questions, which were answered using a score from 1 to 5 (5 corresponds to the best rating): "How satisfied were you with the surgical procedure from start to phacoemulsification? How satisfied were you with the used OVD? How did the OVD help with pupil dilation including insertion of the Malyugin ring? How beneficial was the OVD for the capsulorhexis? How beneficial was the OVD in improving visibility and creating space in the anterior chamber during capsulorhexis?" Afterwards the resulting scores were added and classified (25–23: very good; 22–19: good; 18–16: satisfying; 15–14: sufficient; 13–0: not sufficient). Corrected distance visual acuity (CDVA) was measured preoperatively and 20 h and 4 weeks postoperatively. IOP measurements were performed 3 times (preoperative as well as 6 and 20 h postoperative) using non-contact tonometry (at 6 h) or Goldmann tonometry (at 20 h) and a slit-lamp examination was conducted at each follow-up examination.

Patient demographics and preoperative clinical information are summarized in [Table 1 \[3\]](#). There was no statistically significant difference in patient age between the two groups ($p = 0.805$; Mann-Whitney U test). The pre- and postoperative outcomes regarding IOP, CDVA, operation (OR) time, and OR satisfaction are shown in [Table 2](#). Compared to the control group B (clear OVD), the OR time was statistically significantly lower in group A ($p < 0.001$; Mann-Whitney U test).

Discussion

Trypan blue is commonly used for anterior capsule staining and its efficacy and toxicity have been well studied [4–6]. In the literature, methods have already been described for mixing trypan blue with viscoelastic agents for various purposes, for example, to achieve a limitation of color contact to the region of interest [7]. Kayikioğlu et al. [7] suggested mixing trypan blue with sodium hyaluronate to inject the colored viscoelastic material into the anterior chamber beneath an endothelium-protecting viscoelastic shell before attempting capsu-

lorhexis. The authors concluded that trypan blue mixed in sodium hyaluronate greatly increases the visibility of the anterior lens capsule without significantly touching the adjacent tissues [7]. A comparable technique was described for vitreoretinal surgery with indocyanine green for internal limiting membrane (ILM) staining [8]. Kadonosono et al. [8] showed that this technique was safe and useful in visualizing the ILM, leading to successful ILM removal with minimal retinal damage. However, the preoperative mixing of trypan blue with sodium hyaluronate always involves a risk of contamination, which is why Lanzl and Mertz [9] recommended a different “blue reservoir” technique. With this method, the dye is swept across the capsule from a reservoir behind the iris [9].

In our case series, we demonstrated how the novel blue-colored viscoelastic Pe-Ha-Blue® PLUS improved the OR workflow of cataract surgery in eyes with PXF. Compared to the control group B with clear OVD, our OR time was statistically significantly lower in the Pe-Ha-Blue® PLUS group. With the blue-colored viscoelastics it is possible to fill the anterior chamber with OVD and trypan blue in one single step, which helps to save time and accelerate surgical procedures. Overall, there are 9 necessary steps for a cataract operation with clear OVD and trypan blue in PXF eyes: (1) paracentesis; (2) clear cornea incision; (3) insertion of Supra-*renin*®; (4) insertion of OVD; (5) insertion of Malyugin ring; (6) irrigation of OVD; (7) insertion of trypan blue; (8) irrigation of trypan blue; (9) insertion of OVD. In contrast, only 5 of these steps are required when using Pe-Ha-Blue® PLUS (steps 6–9 are omitted). This increases the effectiveness of the surgical workflow and is particularly interesting for high-volume surgeons or clinics with a high number of cases. In addition, this also increases the safety of the operation, as a shorter overall surgery time can reduce the incidence of complications such as endophthalmitis. With a shorter OR time, we also expect less corneal edema and faster convalescence. This could be one reason why the postoperative CDVA was slightly better in our study group A. Furthermore, there is a positive factor for the patient, because the shorter the OR time, the better the patient’s comfort regarding the local anesthesia effect. In our study, we were able to show that the use of the blue-colored OVD reduced the duration of the first surgical steps from 165 to 112 s (median), which corresponds to a time saving of 53 s for the entire duration of cataract surgery. If the total OR time could be shortened by only 1 min, for example from 7 to 6 min, then this would already correspond to a total time saving of approximately 15%.

The median total OR satisfaction score was 1.50 in our study group A (Pe-Ha-Blue® PLUS) and slightly worse in group B (2.0), but the range of satisfaction ratings was the same in both groups (1.0–3.0). In group A and group B, the overall satisfaction with OR was rated as “very good” or “good” in 88.5% and 73.0% of cases, respectively. Satisfaction with surgery was rated as “satisfying” in 11.5% (group A) and 27.0% (group B). These results show a small advantage in favor of group A, which also confirms our subjective impression in retrospect.

Since Pe-Ha-Blue® PLUS is clearly visible to the surgeon, all OVD residue between the IOL and the posterior capsule can be fully aspirated. This reduces the risk of postoperative IOP elevation, corneal edema, and toric IOL rotation, especially with large-diameter and/or plate-haptic IOLs. The mean IOP was slightly higher in our study group B at 6 and 20 h postoperatively. One reason for this could be either the composition of Pe-Ha-Blue® PLUS or the fact that the OVD residues in study group A could be removed more efficiently and easily.

There are a few more general points about the use of a blue-colored OVD in cataract surgery, which we would like to discuss. In the case of a “vis a tergo” with bursting of the capsule

(Argentinian flag sign) in mature white cataract (“the great white”), the anterior chamber can be refilled with Pe-Ha-Blue® PLUS repeatedly. This allows the blue-colored anterior capsule to be pushed back without the risk of bringing trypan blue into the posterior chamber or the vitreous (through capsular tears or weak zonules) with toxic side effects to the posterior segment. While using Pe-Ha-Blue® PLUS, no additional rinsing with balanced salt solution (BSS) or irrigation/aspiration (I/A) is required. Another point is the management of Synchysis scintillans and vitreous floaters during the operation. By refilling the capsular bag with a blue-colored OVD, the fundus reflex is reduced and shadows of vitreous floaters become less disturbing for the surgeon. This makes the operation much easier and safer, especially removing the cortex, performing the I/A, and polishing the posterior capsule. We recognized another advantage of Pe-Ha-Blue® PLUS in its preferred absorption of ultraviolet light from the microscope, which contributes to the protection of the macula during surgery. In addition, Pe-Ha-Blue® PLUS and a clear standard OVD can be used simultaneously to highlight structures in the eye and achieve better stereoscopic vision, which can be particularly helpful for the education of trainees. One disturbing experience for the surgeon is the occurrence of air bubbles during surgery. With a blue-colored OVD, surgeons can more easily identify air bubbles. Once the air bubble has been aspirated, the areas without OVD are clearly visible and these areas can be refilled to maintain endothelial protection. In principle, we consider blue-colored OVD to be advantageous if unexpected complications occur intraoperatively. In the event of posterior capsule tearing or vitreous loss, Pe-Ha-Blue® PLUS can be useful for staining the posterior capsule without infiltrating the vitreous. This makes the vitreous more visible in the anterior chamber and allows pushing it backwards or performing anterior vitrectomy.

In addition to cataract surgery, we also see application areas for blue-colored OVD in glaucoma or microinvasive glaucoma surgery (MIGS). In corneal surgery, this can lead, for example, to improved visualization of the host cornea, resulting in improved accuracy and safety.

However, there are also some points that the surgeon should consider when using Pe-Ha-Blue® PLUS. On the one hand, Pe-Ha-Blue® PLUS colors the capsule less intensively than standard trypan blue and in exceptional cases of subcapsular posterior cataract in highly myopic eyes with fundus myopicus, visualization during surgery using Pe-Ha-Blue® PLUS may be limited. Moreover, it cannot be used to moisten and protect the exterior part of the eye (conjunctiva and cornea) during surgery, which is sometimes useful and desirable in dry eye syndrome (Sicca).

Our case series shows that the use of a novel blue-colored OVD during cataract surgery in PXF eyes can improve the surgical workflow and make procedures safer and faster. Pe-Ha-Blue® PLUS seems to be a helpful alternative to clear OVD especially in challenging cases. Though PXF syndrome and cataracts can routinely be performed without the use of hooks or rings and without staining the capsule, in case of need, this new blue-colored OVD seems to be a significant innovation. In our opinion, it is a useful agent for both rookies and high-volume surgeons.

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tion (Malyugin ring). These applications are bringing enjoyment to our work, improve the OR workflow and safety! Therefore, we can follow our pleasure performing surgeries.

Statement of Ethics

The current study adhered to the tenets of the Declaration of Helsinki and all patients gave their written informed consent to publish their case.

Disclosure Statement

The authors have no conflicts of interest to declare.

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| | Pe-Ha-Blue® PLUS | POLYHYL® 1.6% |
|--|---|--|
| |  |  |
| Sodium hyaluronate | 1.7% | 1.6% |
| Molecular weight [mio. Daltons] | 1.1 – 2.0 | 1.2 – 2.0 |
| Osmolality [mOsm/kg] | 270 – 400 | 270 – 400 |
| pH | 6.8 – 7.4 | 6.8 – 7.5 |
| Source | bacterial fermentation | |
| Sodium hyaluronate / ml | 17.000 mg | 16.000 mg |
| Sodium chloride / ml | 8.500 mg | 8.500 mg |
| Disodium hydrogen phosphate dihydrate / ml | 0.563 mg | 0.563 mg |
| Sodium dihydrogen phosphate dihydrate / ml | 0.045 mg | 0.045 mg |
| Trypan blue / ml | 0.020 mg | 0.0 mg |

Fig. 1. Specifications of the two ophthalmic viscoelastic devices compared in our case series.

Table 1. Preoperative patient information

| | Group A (Pe-Ha-Blue® PLUS) | Group B (clear OVD) |
|---|-------------------------------|------------------------|
| Patients, <i>n</i> | 26 | 26 |
| Eyes, <i>n</i> | 26 | 26 |
| Age, years | | |
| Mean ± SD | 73.5±8.3 | 74.2±7.5 |
| Median (range) | 74.5 (56–88) | 75.0 (56–88) |
| Female, % | 53.8 | 61.5 |
| Male, % | 46.2 | 38.5 |
| Lens Opacities Classification (LOCS III), % | | |
| NC3 | 11.5 | 11.5 |
| NC4 | 15.4 | 11.5 |
| NC5 | 3.8 | 19.2 |
| NC6 | 15.4 | 7.7 |
| C2 | 7.7 | 7.7 |
| C3 | 11.5 | 7.7 |
| C4 | 7.7 | 7.7 |
| C5 | 3.8 | 7.7 |
| P2 | 0.0 | 3.8 |
| P3 | 15.4 | 7.7 |
| P4 | 3.8 | 3.8 |
| P5 | 3.8 | 3.8 |

Cataracta senilis is graded according to the Lens Opacities Classification System III (LOCS III) [3].
NC, nuclear color; C, cortical cataract; P, posterior subcapsular cataract.

Table 2. Pre- and postoperative outcomes of IOP, CDVA, OR time, and OR satisfaction in both groups

| | Group A (Pe-Ha-Blue® PLUS) | Group B (clear OVD) |
|-----------------------------|-------------------------------|------------------------|
| IOP preop, mm Hg | | |
| Mean ± SD | 17.5±2.7 | 17.9±2.6 |
| Median (range) | 17.0 (13.0–24.0) | 18.0 (14.0–25.0) |
| IOP 6 h postop, mm Hg | | |
| Mean ± SD | 17.9±2.3 | 18.5±2.8 |
| Median (range) | 17.5 (14.0–23.0) | 18.0 (14.0–26.0) |
| IOP 20 h postop, mm Hg | | |
| Mean ± SD | 15.2±1.3 | 16.2±1.5 |
| Median (range) | 15.0 (13.0–19.0) | 16.0 (14.0–19.0) |
| CDVA preop, logMAR | | |
| Mean ± SD | 0.40±0.24 | 0.38±0.21 |
| Median (range) | 0.30 (0.10–1.00) | 0.35 (0.10–1.00) |
| CDVA 20 h postop, logMAR | | |
| Mean ± SD | 0.19±0.11 | 0.21±0.11 |
| Median (range) | 0.15 (0.05–0.52) | 0.22 (0.10–0.40) |
| CDVA 4 weeks postop, logMAR | | |
| Mean ± SD | 0.05±0.06 | 0.07±0.06 |
| Median (range) | 0.05 (0.00–0.22) | 0.07 (0.00–0.22) |
| OR time ¹ , s | | |
| Mean ± SD | 113.6±8.2 | 165.6±8.2 |
| Median (range) | 112.0 (99.0–129.0) | 165.0 (145.0–178.0) |
| OR satisfaction total score | | |
| Median (range) | 1.50 (1.0–3.0) | 2.0 (1.0–3.0) |
| Satisfaction with OR, n (%) | | |
| Very good | 13 (50.0) | 6 (23.0) |
| Good | 10 (38.5) | 13 (50.0) |
| Satisfying | 3 (11.5) | 7 (27.0) |
| Sufficient | 0 (0) | 0 (0) |
| Not sufficient | 0 (0) | 0 (0) |

IOP, intraocular pressure; preop, preoperative; postop, postoperative; CDVA, corrected distance visual acuity; OR, operation. ¹ Time from start of surgery to beginning of phacoemulsification.