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WHITE PAPER
VISCOELASTICS – Pe-Ha-Visco®

CLINICAL OBSERVATION ON SAFETY AND PERFORMANCE OF THE VISCOELASTIC DEVICE PE-HA-VISCO® APPLIED DURING OPHTHALMIC SURGERIES

FINAL REPORT
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Key Highlights

- Ophthalmic viscoelastic devices (OVDs) are commonly used during cataract surgery to maintain the pressure in the anterior chamber and to protect the corneal endothelium from being damaged.
- Pe-Ha-Visco® OVD is an injectable transparent gel, sterile and isotonic, based on hydroxypropyl-methylcellulose (HPMC) as the main component.
- In this observational study, the safety and efficacy of Pe-Ha-Visco® used in two different concentrations (2.0% and 2.4%) were assessed. Pe-Ha-Visco® was applied during routine cataract surgery in 77 eyes, and the follow-up was 1-day after surgery.

Background & Aim

Ophthalmic viscoelastic devices (OVDs) are used during cataract surgery as they offer numerous advantages. OVDs aim to maintain the pressure in the anterior chamber during surgery in order to keep the intervention safe; they also protect the corneal endothelium and facilitate the surgical procedure. However, OVDs have longer retention time in the eye after surgery which is known to cause a significant increase in postoperative intraocular pressure (IOP) – this occurs irrespective of the OVD type used.[1,2,3,4,5] This is because traces of OVD left in the eye can obstruct the trabecular meshwork, affecting the aqueous outflow and resulting in IOP spikes within 24 hours after surgery. This is of particular concern for patients with glaucoma. Therefore, removal of OVD is essential to avoid IOP spikes.

Early research work already demonstrated the advantages of protecting the corneal endothelium and improving control of the anterior chamber during surgery. Today, there is a choice of OVDs available on the market with different chemical and physical properties, and research and clinical applications continue to expand our understanding of how OVDs work and how they can be utilized to improve surgical outcomes.

OVDs are commonly classified in 2 main categories depending on their rheologic properties: lower viscosity dispersive and higher viscosity cohesive. Dispersive OVDs are low viscosity materials with good adhesion properties to intraocular structures and instruments. They provide excellent protection for the corneal endothelium during surgery, however, due to their short molecular chains they are fragile and therefore more difficult to remove at the end of surgery. Cohesive OVDs are highly viscous materials with intramolecular adhesion and entanglement. They are ideal for creating and maintaining spaces during ocular surgeries and are easier to remove. However, they offer a lower corneal protection.

This report provides clinical data on the safety and performance of the OVD Pe-Ha-Visco® from Albomed® (Albomed GmbH, Schwarzenbruck, Germany). Pe-Ha-Visco® is based on hydroxypropyl-methylcellulose (HPMC) and due to its physical properties, it is classified as a dispersive viscoelastic.
In order to assess the safety of OVD use, it is important to evaluate the occurrence of side effects and in particular increase of intraocular pressure post-operatively; the efficacy of the OVD is assessed by investigating the time it takes for the surgeon to perform the procedure.

Specifications of Pe-Ha-Visco®

Intended purpose

The intended purpose of Pe-Ha-Visco® HPMC OVDS is the retention of the anterior chamber, and the lubrication and protection of ocular tissues during intraocular surgery. Pe-Ha-Visco® reduces the danger of traumatization of the corneal endothelium, the iris, and the ciliary body by direct contact with surgical instruments.

Indications

Pe-Ha-Visco® serves as a volume substitute and as adjuvant for the following operations:

- Cataract surgery with or without intraocular lens implantation
- Glaucoma surgery
- Corneal surgery

Description

The range of Pe-Ha-Visco® HPMC intraocular gel products from Albomed® comprises 2 devices, each with the following properties:

- Injectable transparent gel
- Based on hydroxypropylmethylcellulose (i.e. not animal origin)
- HPMC concentration of 2.0% or 2.4%
- Packaged in 2.25ml borosilicate glass syringes in a volume of 2 ml
- Equipped with a suitable backstop and plunger rod in the syringe
- Supplied with a sterile single use cannula
- Provided in secondary packaging in a blister that protects the integrity of each syringe
- Can be stored at room temperature protected from light for 42 months

Composition

The following Table 1 summarizes the composition of Pe-Ha-Visco® OVDs.

Table 1 Composition of Pe-Ha-Visco®

Ingredient	Specification acc. to current edition of European Pharmacopoeia	Unit formula for 1ml
Hydroxypropylmethylcellulose	Ph. Eur.Monograph < 0348 > "Hypromellose (type 2910)"	20.0 mg to 24.0 mg (2.0%-2.4%)
Sodium Chloride (NaCl)	Ph. Eur. <0193> „Sodium chloride"	6.4 mg
Potassium Chloride (KCl)	Ph. Eur. <0185> „Potassium chloride"	0.75 mg
Calcium chloride (CaCl2 2 H_2O)	Ph. Eur. <0015> „Calcium chloride dihydrate"	0.48 mg
Magnesium chloride (MgCl2 6 H_2O)	Ph. Eur. <0402> „Magnesium chloride hexahydrate"	0.30 mg
Sodium acetate ($C_2H_3NaO_2$ 3 H_2O)	Ph. Eur. <0411> „Sodium acetate trihydrate"	3.9 mg
Sodium citrate ($C_6H_5Na_3O_7$ 2 H_2O)	Ph. Eur. <0412> „Sodium citrate"	1.7 mg
WFI Water For Injection	Ph. Eur. <0169> „Water for Injection"	q.s. 1 ml

Specifications

The following Table 2 gives an overview of the specifications of both HPMC OVD products from Albomed®.

Table 2 Specifications of HPMC Intra-Ocular Gel products

Analysis	Method	Specifications of HPMC INTRA-OCULAR GEL products	
		INTRA-OCULAR 2.0%	INTRA-OCULAR 2.4%
Appearance	Visual	Colourless, transparent, no visible foreign matter	
HPMC content	Eur.Ph. monograph <0348> and <2.2.25>	1.85-2.10%	2.28-2.64%
Endotoxins	Eur.Ph. <2.6.14.>	< 0.2 U.I./ml	
Sterility of the gel inside the syringe	Eur.Ph. <2.6.1.>	Sterile	
Sterility on the outside surface of the syringe	Eur.Ph. <2.6.1.>	Sterile	
pH	Eur. Ph. <2.2.3>	6.8 – 7.5	
Viscosity	Eur. Ph. <2.2.10> and <2.2.8>	2600-7000 cP	4500-10000 cP
Osmolarity	Eur. Ph. <2.2.35>	270 – 400 mOsmol/kg	
Particles per container	Eur. Ph. <2.9.19>	> 10 µm: 25 000/syringe > 25 µm: 5 000/syringe	
U.V. transparency	Eur. Ph. <2.2.25>	Conform (no absorption)	
Volume	Eur. Ph. <2.9.17>	To nominal filling volume of syringe	

Clinical Data

Study design

An open, non-interventional, monocentric study was performed in order to evaluate safety and efficacy of the Pe-Ha-Visco® OVD from Albomed®. Lead investigator was MD Ch. Winkler von Mohrenfels and the study was performed at his private clinic (Neutraubling, Germany).

Purpose

The main purpose of this observation was to assess the safety and efficacy of the Pe-Ha-Visco® when applied according to its intended purpose for cataract surgery.

Study endpoints

The performance of Pe-Ha-Visco® was assessed according to the following endpoints:

- Duration of the treatment (treatment time)
- Intraocular pressure (IOP) in mmHg: this was recorded 1 day after surgery
- Absence of OVD between the intraocular lens (IOL) and the posterior capsule: OVD molecules remaining after aspiration could block the trabecular meshwork and result in an IOP increase
- Absence of OVD in the anterior chamber: no OVD molecules should remain in the anterior chamber after aspiration
- Corneal transparency: corneal transparency should be maintained. An opacification of the cornea can occur after an ocular intervention if the corneal endothelium has been damaged during surgery, or as a result of inflammation or infection.

Study visits

There was one follow-up visit 1-day after cataract surgery (as per standard cataract surgery follow-up).

Results

In total, 77 eyes were included in the study: 34 right eyes and 43 left eyes.
Out of these 77 eyes, 19 eyes received Pe-Ha-Visco® in a concentration of 2.0%, and 58 eyes received Pe-Ha-Visco® 2.4% (Table 3).

Table 3 Distribution of devices used

Product	Number of eyes (n)	Percentage of eyes (%)
Pe-Ha-Visco® 2.0%	19	24.7
Pe-Ha-Visco® 2.4%	58	77.3
Total	77	100.0

Efficacy: Duration of treatment (in minutes)

On average, treatment time was 11.66 minutes, ranging from 8 to 25 minutes for all eyes together. As shown on Table 4, duration was approximately equal for both groups.

Table 4: Treatment duration (in minutes)

	Treatment Duration (min)		
	All eyes (n=77)	Pe-Ha Visco® 2.0% (n=19)	Pe-Ha Visco® 2.4% (n=58)
Mean ± SD	11.66 ± 3.18	11.32 ± 2.25	11.78 ± 3.41
Range	8 to 25	8 to 16	8 to 25

Safety: IOP (in mmHg)

On average, the IOP measured at the 1-day postoperative visit was 15.7 mmHg, ranging from 8 to 28 mmHg for all eyes together. As shown on Table 5, the mean postoperative IOP was slightly greater for the group treated with the higher concentration of 2.4%, but within normal range.

Table 5: IOP values at the 1-day postoperative visit (in mmHg)

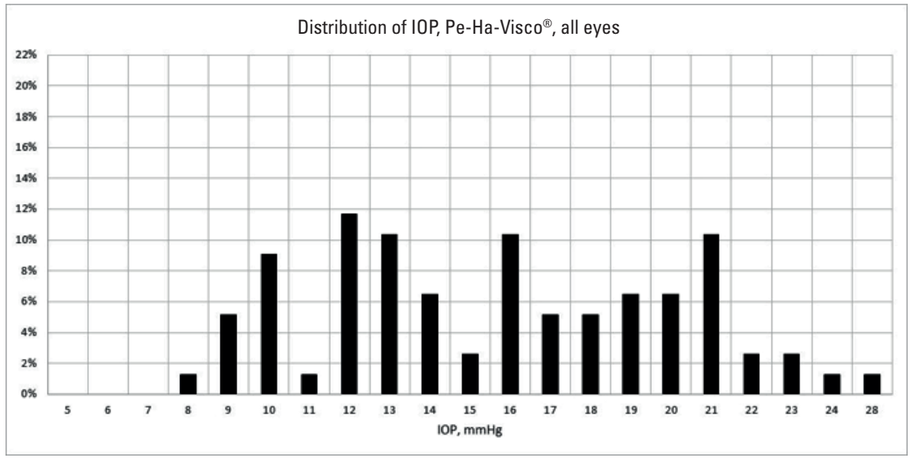
	IOP (mmHg)		
	All eyes (n=77)	Pe-Ha Visco® 2.0% (n=19)	Pe-Ha Visco® 2.4% (n=58)
Mean ± SD	15.71 ± 4.40	14.05 ± 3.62	16.26 ± 4.50
Range	8 to 28	8 to 20	9 to 28

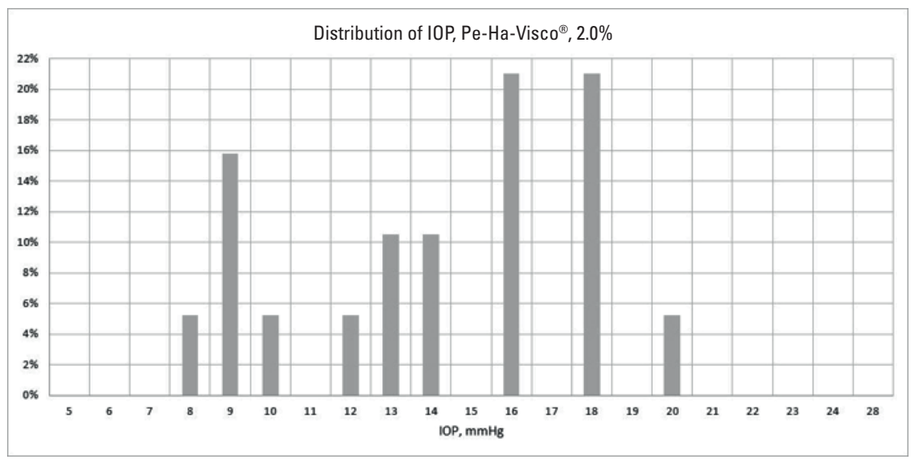
The distribution of IOP values at day-1 is shown in Table 6 and Figure 1. Assuming that the normal distribution of IOP ranges from 10 mmHg to 21 mmHg, none of the eyes treated with Pe-Ha-Visco® 2.0% had an IOP above 21 mmHg. In total, 6 eyes (10%) treated with Pe-Ha-Visco® 2.4% had an IOP greater than 21 mmHg, with 5 eyes between 22 mmHg and 24 mmHg and only 1 eye with 28 mmHg.

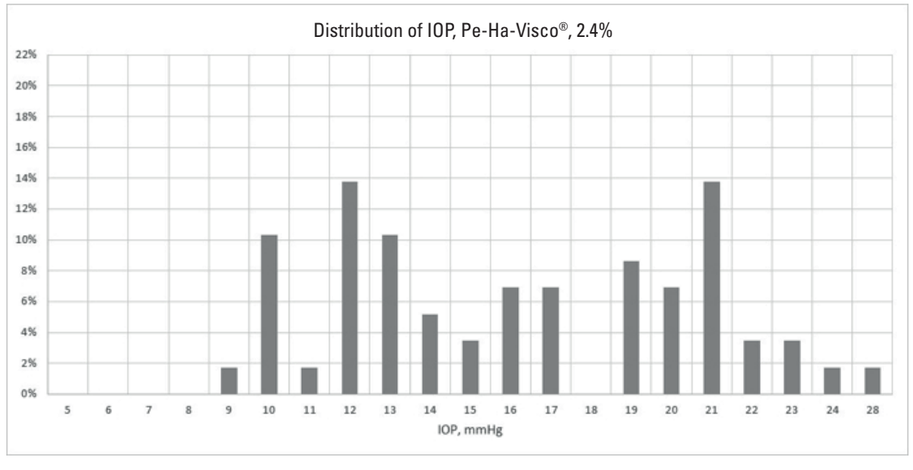
Table 6: Frequency of IOP values per concentration

	All eyes	Eyes treated with Pe-Ha Visco® 2.0%	Eyes treated with Pe-Ha Visco® 2.4%	All eyes	Eyes treated with Pe-Ha Visco® 2.0%	Eyes treated with Pe-Ha Visco® 2.4%
IOP value	Frequency (n)			Frequency (n)		
8	1	1	0	1.30%	5%	0%
9	4	3	1	5.19%	16%	2%
10	7	1	6	9.09%	5%	10%
11	1	0	1	1.30%	0%	2%
12	9	1	8	11.69%	5%	14%
13	8	2	6	10.39%	11%	10%
14	5	2	3	6.49%	11%	5%
15	2	0	2	2.60%	0%	3%
16	8	4	4	10.39%	21%	7%
17	4	0	4	5.19%	0%	7%
18	4	4	0	5.19%	21%	0%
19	5	0	5	6.49%	5%	9%
20	5	1	4	6.49%	0%	7%
21	8	0	8	10.39%	0%	14%
22	2	0	2	2.60%	0%	3%
23	2	0	2	2.60%	0%	3%
24	1	0	1	1.30%	0%	2%
28	1	0	1	1.30%	0%	2%
∑	77	19	58	100.00%	100.00%	100.00%

Figure 1: Distribution of IOP values 1-day postoperatively
for all eyes (black bars), for eyes treated with the 2.0% concentration (light grey bars) and for eyes treated with the 2.4% concentration (dark grey bars)







Safety

Traces of OVD:

In all 77 eyes there were no OVD traces visible between the IOL and the posterior capsule. Additionally, no residues of OVD were visible in the anterior chamber.

Corneal transparency:

Out of all 77 eyes, corneal edema was reported in only 1 eye (1.3%) treated with the Pe-Ha-Visco® 2.0%.

Additional follow-up visits

No other additional follow-up visits were required for any patient.

Summary and Conclusion

The present study was able to confirm the efficacy and safety of the Pe-Ha-Visco® product line in the field.

Several OVDs are available on the market and numerous prospective randomized control trials have been conducted to compare safety, efficacy, and performance of various OVDs used during routine small-incision cataract surgeries and IOL implantation. A recent meta-analysis by Malvankar-Mehta et al[1] demonstrated that there was a nonsignificant increase in postoperative IOP at the 1-day follow-up with HPMC 2%. This is in agreement with our findings where IOP was within normal limits [6,7] (14.05 ± 3.62, ranging from 8 to 20 mmHg).

Some studies have shown that within a family of molecularly similar OVDs, lower viscosity OVDs appeared to cause slightly lower mean elevations in IOP in normal patients at 24 hours.[8] This appeared to be the case in this study, where none of the eyes treated with Pe-Ha-Visco® 2.0% had an IOP of 21 mmHg or above whereas 10% of eyes treated with Pe-Ha-Visco® 2.4% had an IOP above 21 mmHg at the 1-day postoperative visit. However, this is not unusual for ophthalmologic surgery. Published scientific literature reported that a 1-day postoperative IOP of 30 mmHg or higher occurs under normal conditions in about 2% treatments.[9,10] None of the eyes had an IOP of 30 mmHg or above in our sample. Additionally, none of the eyes were diagnosed with ocular hypotony. This demonstrates the safety of Albomed® Pe-Ha-Visco® OVD products.

Safety was confirmed by the fact that no traces of OVD were visible in any of the study eyes postoperatively, and corneal transparency was maintained in all eyes.

In terms of efficacy, treatment duration was found to be approximately the same for both HPMC concentration groups and within the average reported values in the literature.[11]

References

1 Malvankar-Mehta M,Fu A, Subramanian Y, Hutnik C. Impact of Ophthalmic Viscosurgical Devices in Cataract Surgery. J Ophthalmol. 2020: Oct 20 - doi: 10.1155/2020/7801093.

2 Rainer G, Schmid K. E, Findl O. Natural course of intraocular pressure after cataract surgery with sodium hyaluronate 1% versus hydroxypropylmethylcellulose 2%," Ophthalmology. 2007; 114(6): 1089–1093.

3 Rainer G, Menapace R, Findl O, Georgopoulos M, Kiss B, Petternel V. Intraocular pressure after small incision cataract surgery with Healon5 and Viscoat. J Cataract Refract Surg. 2000; 26(2): 271–276.

4 Holzer M P, Tetz M R, Auffarth G U, Welt G U, Völcker H E. Effect of Healon5 and 4 other viscoelastic substances on intraocular pressure and endothelium after cataract surgery. J Cataract Refract Surg. 2001 Feb;27(2):213-8.

5 Rainer G, Menapace R, Findl O. Intraocular pressure rise after small incision cataract surgery: a randomised intraindividual comparison of two dispersive viscoelastic agents. British J Ophthalmol. 2001; 85(2): 139–142.

6 James C. Tsai. High Eye Pressure and Glaucoma, October 29, 2017, accessed on November 23, 2020 at https://www.glaucoma.org/gleams/high-eye-pressure-and-glaucoma.php

7 American Academy of Ophthalmology, Intraocular pressure, Accessed on November 23, 2020 at https://www.aao.org/bcscsnippetdetail.aspx?id=f010bbf6-3f3e-486b-b5cd-0ad86ddb9d74

8 Arshinoff SA, Albiani DA, Taylor-Laporte J. Intraocular pressure after bilateral cataract surgery using Healon, Healon5, and Healon GV, J Cataract Refract Surg 2002; 28:617–625.

9 Gupta A, Vernon SA. Is the 1-day postoperative IOP check needed post uncomplicated phacoemulsification in patients with glaucoma and ocular hypertension? Eye (2015) 29, 1299–1307.

10 Bonnell, SooHoo, Seibold, et al. One-day postoperative intraocular pressure spikes after phacoemulsification cataract surgery in patients taking tamsulosin, J Cataract Refract Surg 2016; 42:1753–1758.

11 Rothschild P-R, Grabar S, Le Dû B, et al., Patients' subjective assessment of the duration of cataract surgery: a case series. BMJ Open 2013

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