Subconjunctival implantation of ologen Collagen Matrix to treat ocular hypotony after filtration glaucoma surgery

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Abstract

Purpose To report the results of subconjunctival ologen Collagen Matrix implantation to manage ocular hypotony after filtration glaucoma surgery.

Patients and methods This retrospective observational case series included 12 consecutive implantations of ologen in nine eyes of nine Japanese subjects (five men, four women; mean age $\pm$ SD, 72.1 ± 12.7 years) who underwent subconjunctival implantation of the device to treat hypotony after glaucoma filtration surgery. Demographic data and surgical results were collected by chart review. **Results** The subjects included six patients who underwent trabeculectomy and three who underwent an EX-PRESS shunt surgery. The duration between the last glaucoma surgery and the initial ologen implantation was longer than 2 years in seven (78%) eyes. Bleb leakage in five (56%) eyes preoperatively stopped in all cases by 8 days after the device implantation. After the initial implantation, three (33.3%) eyes required a second implantation of ologen because of insufficient efficacy. After a mean follow-up of 12.6 ± 6.8 months, the mean preoperative intraocular pressure (IOP) of 3.8 ± 2.7 mmHg increased significantly ($P = 0.0001$) to 9.0 ± 3.2 mmHg; no eye required glaucoma medication to control the IOP. No vision-threatening complications developed in association with the treatment.

Conclusion When conservative management failed, subconjunctival implantation of ologen Collagen Matrix in combination with bleb revision can be a useful therapeutic option for ocular hypotony after glaucoma filtration surgery.

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Introduction

Ocular hypotony after glaucoma filtering surgery becomes sight threatening because of hypotony maculopathy and bleb infection, especially when a leaking or avascular bleb is evident;^{1,2} after trabeculectomy (LEC) with adjunctive mitomycin C (MMC), bleb oozing occurs in 11.9–35.8%, bleb leakage in 2.0–5.6%, and hypotony maculopathy in 1.3–20%.^{3–5} Treatment options for overfiltration and/or leaking blebs include conservative management of topical autologous serum,⁶ bleb injection of autologous blood,⁷ or viscoelastic material,⁸ and anterior chamber injection of viscoelastic material⁹ or gas.¹⁰ Surgical management includes transconjunctival flap suturing,^{11,12} excision of thin/leaking blebs and conjunctival advancement,^{5,13} patch grafting using donor sclera,^{14,15} donor cornea,¹⁶ and autologous conjunctiva.¹⁷ Although conservative management usually has little long-lasting effect,¹³ techniques to reduce the transscleral flow by suturing or tissue patching can lead to massive elevation of the intraocular pressure (IOP), necessitating further IOP-lowering interventions.¹⁸

Ologen Collagen Matrix (Aeon Astron Europe B.V., Leiden, The Netherlands) is a sponge-like surgically implantable device that, according to the manufacturer, contains a connected porous structure of 10- to 300- μ m diameter of cross-linked lyophilized porcine type I atelocollagen ($\geq 90\%$) and glycosaminoglycans ($\leq 10\%$). In a rabbit model of LEC, subconjunctival placement of ologen prevented surgical failure by maintaining the sizes of the blebs.¹⁹ A clinical study reported that adjunctive use of ologen for LEC might be comparable to MMC for LEC in IOP-lowering efficacy, reduction in the number of glaucoma medications, success rates, and

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tolerability.²⁰ However, another study concluded that ologen for LEC could not possibly achieve the surgical success rate and IOP reduction achieved with MMC for LEC.²¹ In addition, use of ologen compared with LEC alone was associated with slightly higher IOP 1 year postoperatively.²²

Although the efficacy of ologen use for LEC in reducing IOP remains inconclusive, it has been reported consistently that the morphology of the filtering blebs after ologen–LEC showed reduced avascularity compared with MMC–LEC and few of the expected side effects such as allergy to the implant or implant dislocation.^{23,24} In an animal model, ologen effectively enhanced the closure of conjunctival defects via its role as a three-dimensional scaffold for cellular migration and proliferation; therefore, it was expected to be useful to repair postoperative bleb leaks.¹⁹ These studies prompted us to use ologen to manage hypotony and/or bleb leakage after filtration surgeries. We report our experience with subconjunctival implantation of ologen in Japanese subjects with ocular hypotony.

Materials and methods

This observational case series included 12 consecutive cases of ologen implantation in nine eyes of nine Japanese subjects (five men, four women; mean age $\pm$ SD, 72.1 ± 12.7 years) who underwent subconjunctival implantation of the device to treat hypotony after glaucoma filtration surgery at Matsue Red Cross Hospital between June 2015 and December 2016. The study adhered to the tenets of the Declaration of Helsinki; the institutional review board of Matsue Red Cross Hospital reviewed and approved the research. Preoperatively, all subjects provided written informed consent to undergo surgery and for the use of clinical data regarding the results obtained during the follow-up period. Subjects' data and surgical results were collected by reviewing the medical charts. We report two representative cases of the use of ologen Collagen Matrix in eyes with hypotony.

Surgical procedure

One surgeon (MT) performed all surgeries (Supplementary Video 1). Standard sub-Tenon anesthesia was induced using 2% lidocaine. The adhesion between the sclera and conjunctiva around the bleb was dissected through a small conjunctival peritomy made away from the bleb using a spring scissors or needling knife (Bleb Knife II, Kai Industries, Gifu, Japan) to release pressure inside the bleb and form a subconjunctival space for implantation. The ologen Collagen Matrix (model 862051, 12 mm in diameter $\times$ 1 mm thick) was placed beneath the bleb using Gaskin forceps (Geuder, Heidelberg,

Germany); when inserted, the ologen was folded to fit the size of the bleb and conjunctival entry. The conjunctiva was closed with a 10-0 polyglactin suture. At the end of surgery, 1.65 mg of dexamethasone sodium phosphate (Decadron, Aspen Japan, Tokyo, Japan) was injected subconjunctivally and 0.3% ofloxacin ointment (Tarivid, Santen Pharmaceutical, Osaka, Japan) was applied. Finally, 1.5% levofloxacin (Nipro, Osaka, Japan) and 0.1% betamethasone (Sanbetason, Santen Pharmaceutical) were applied topically four times daily for 3–4 weeks postoperatively in all cases.

Results

The subjects' demographic data and surgical results are summarized in Table 1. The subjects included six who had undergone a LEC and three who had undergone EX-PRESS shunt (Alcon Japan, Tokyo, Japan) surgeries. MMC was used in all the eyes except one (case 7, use of MMC unknown) during the last filtration surgery. The duration between the last glaucoma surgery and the initial ologen implantation was longer than 2 years in seven (78%) eyes. Before the initial implantation, the treatments that failed included viscoelastic injection into the anterior chamber in four (44%) eyes, conjunctival suturing in two (22%) eyes, transient coverage of the leak point by posterior conjunctiva in one (11%) eye, and topical autologous serum use in one (11%) eye. Two (22%) eyes had a history of a bleb infection. A bleb leak occurred in five (56%) eyes; the leakage stopped in all cases by 8 days after the implantation. After the initial implantation, three (33.3%) eyes required a second implantation (cases 1 and 8 for recurrence of bleb leakage and case 4 for insufficient increase in the IOP). After a mean follow-up of 12.6 ± 6.8 months, the mean preoperative IOP of 3.8 ± 2.7 mmHg increased significantly ($P=0.0001$ by the paired *t*-test) to 9.0 ± 3.2 mmHg. No eye required glaucoma medication to control the IOP. No vision-threatening complication developed in association with the surgery, and the best-corrected visual acuity (BCVA) did not decrease at the last follow-up visit, except for one eye in which the BCVA decreased because of glaucoma progression (case 3).

Discussion

In this case series, all eyes with hypotony were managed successfully by subconjunctival implantation of ologen even after conventional management procedures failed. Previously, successful management of hypotony after MMC–LEC was reported in a case series of 12 eyes.¹⁸ Ologen was used as a patch graft to treat one case of tube erosion after implantation of a Baerveldt glaucoma device²⁵ and two cases of scleral necrosis after pterygium

Table 1 Summary of cases

Case	Age (years)	Sex	Eyes	Glaucoma type	Last glaucoma surgery	Bleb leakage	Treatments before ologen implantation	Duration between last glaucoma surgery and ologen implantation	Preoperative				Last follow-up			Follow-up after first ologen implantation	Comments
									Preoperative		Bleb leakage stopped	Bleb leakage recurred	Last follow-up				
									BCVA	IOP (mmHg)			BCVA	IOP (mmHg)	Glaucoma medication		
1a	79	M	L	POAG	LEC	Yes	Conjunctival suture, four times	4 Years	0.7	1	POD5	POM4	1.0	8	No	19 Months	Ologen was implanted a second time at POM5 due to recurrence of bleb leakage
1b						Yes			1.0	3	POD1	None					Macular folds resolved
2	83	F	L	PEG	LEC	No	Viscoelastic injection, two times	11 Years	0.3	2	–	–	0.8	5	No	21 Months	Descemet's folds and macular folds resolved
3	54	F	R	POAG	EXP	Yes	Topical autoserum	2 Months	0.2	3	POD8	None	0.1	12	No	16 Months	VA decreased due to glaucoma progression
4a	82	F	R	UG	LEC	No	Viscoelastic injection	12 Years	0.08	1	–	–	0.2	7	No	15 Months	Ologen was implanted a second time at POM4 due to insufficient rise in IOP
4b						No			0.08	4	–	–					Macular folds resolved
5	87	M	R	PEG	EXP	No	Viscoelastic injection	2 Years	0.08	2	–	–	0.1	6	No	17 Months	Choroidal detachment resolved
6	65	M	R	POAG	LEC	No	Viscoelastic injection, three times	6 Years	0.5	5	–	–	0.6	7	No	13 Months	Macular folds resolved
7	81	M	L	POAG	LEC	Yes	Antibiotics for bleb infection	9 Years	0.7	9	POD1	None	0.8	14	No	4 Months	
8a	61	M	R	POAG	LEC	Yes	Antibiotics for bleb infection	6 Years	0.6	6	POD1	POM2	0.5	13	No	5 Months	Ologen was implanted a second time at POM3 due to bleb leakage
8b						Yes											
9	57	F	L	POAG	EXP	Yes	Conjunctival suture	1 Month	0.5 0.4	9 5	POD1 POD2	None None	0.6 0.4	9	No	3 Months	

Abbreviations: EXP, EX-PRESS shunt with intraoperative mitomycin C use; F, female; IOP, intraocular pressure; L, left; LEC, trabeculectomy with intraoperative mitomycin C use (intraoperative mitomycin C use is unknown for case 7); M, male; PEG, pseudoefferation glaucoma; POAG, primary open-angle glaucoma; POD, postoperative day; POM, postoperative month; UG, uveitic glaucoma; viscoelastic injection, VA, best-corrected visual acuity; Viscoelastic injection, viscoelastic injection into anterior chamber.

excision.²⁶ Taken together with previous reports, we confirmed the efficacy of ologen for treating hypotony via its role in wound-healing modulation. In a previous report,¹⁸ additional compression sutures and a pericardium patch were applied for persistent hypotony after the failure of initial ologen implantation, thus use of second ologen is unique in the literature. In addition to this, use of ologen for treating hypotony after EX-PRESS shunt also is unique in the literature. In a previous report,¹⁸ an avascular leaking area of conjunctiva was resected and the neighboring conjunctiva was readapted; postoperative ologen exposure occurred in one eye and use of an antiglaucoma medication due to increased IOP was required in two eyes in a previous case series. We left an avascular area of the conjunctiva unresected; thus, the difference in the surgical procedure might explain why we did not experience postoperative ologen exposure and excessive IOP increases in the current case series, but this remains inconclusive.

Compared with MMC use, fewer sutures or looser closure of the scleral flap is recommended when ologen is used with LEC²³ or EX-PRESS shunt implantation,²⁷ because ologen restricts transscleral flow in the early postoperative period. This might explain why the bleb leakage stopped in the early postoperative period in the current cases. According to the manufacturer, the device should completely degrade within 90–180 days, although previous reports have indicated that ologen might degrade only partially 6 months after implantation,²⁴ or could be observed by ultrasound biomicroscopy 9 months after implantation²⁸ when the thicker model (7 mm in diameter and 4 mm thick) was implanted. Accordingly, progression of the degradation process seemed associated with the bleb leakage that recurred at 4 months (case 1) and 2 months (case 8) after the initial implantation of the thinner model (1 mm thick) in our case series.

When ologen was placed into the subconjunctival space, the histopathologic examination showed that myoblasts proliferated randomly and secreted connective tissue in the Collagen Matrix during the wound-healing process, and the myofibroblasts and vascularization were expected to completely replace the implant in the long term.^{21,26} After ologen implantation, the avascular blebs typically converted to more vascularized bleb with a thicker bleb wall (Supplementary Information Case 1 and 2). Optical coherence tomography showed that this accompanied complete degradation of ologen and a thick supportive tissue formed beneath the bleb wall (Supplementary Information Case 2). Accordingly, as expected previously,¹⁹ providing a three-dimensional scaffold for cellular migration and proliferation was likely the mechanism underlying the efficacy of subconjunctival ologen implantation to treat hypotony in the current case series. It is noteworthy that the entire bleb wall thickened

(Supplementary Information Case 2) even though the ologen was uniformly located beneath the bleb wall in the early postoperative period (Supplementary Information Case 2). Thus, soluble factors, such as the collagen components, released from the ologen itself or cytokines released from the cells that proliferated into the bleb might be associated with formation of a thick bleb, but that remains to be confirmed.

The limitations of the current study included the absence of a control group, retrospective study design, and short follow-up. When the ologen was implanted, we dissected the scar tissue around the bleb; thus, we cannot exclude the possibility that release of pressure inside the bleb and accompanying bleeding in the bleb was associated with resolution of the hypotony and bleb leakage independent of the ologen implantation in the current case series. However, since we did not observe any surgical complications related specifically to ologen, we believe that simultaneous use of ologen in combination with the bleb revisions reported here is worth considering when treating hypotony after glaucoma filtration surgery.

Summary

What was known before

- A single case series reported the usefulness of subconjunctival implantation of ologen Collagen Matrix to manage ocular hypotony after LEC.

What this study adds

- This case series reproduced the efficacy of subconjunctival implantation of ologen Collagen Matrix to manage ocular hypotony after LEC and EX-PRESS shunt implantation.
 - A second implantation of ologen is effective when the initial implantation is not adequate.
 - Avoiding resection of an avascular bleb area when ologen is implanted can be associated with less chance of development of surgical complications such as postoperative device exposure.
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Conflict of interest

The ologen Collagen Matrix used in this study was provided by Body Organ Biomedical Corporation, Taipei, Taiwan.

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