The Literature

BY SARAH KHODADADEH, MD

USING A COLLAGEN MATRIX IMPLANT (OLOGEN) VERSUS MITOMYCIN-C AS A WOUND HEALING MODULATOR IN TRABECULECTOMY WITH THE EX-PRESS MINI GLAUCOMA DEVICE: A 12-MONTH RETROSPECTIVE REVIEW

Johnson MS, Sarkisian SR Jr¹

ABSTRACT SUMMARY

In this retrospective study, Johnson and Sarkisian reported 12-month clinical results for the success and complication rates of patients undergoing trabeculectomy with the Ex-Press Glaucoma Filtration Device (Alcon Laboratories, Inc.) using a collagen matrix implant (Ologen; Optous) compared to those of patients undergoing the same procedure using mitomycin C (MMC).¹

A single surgeon performed a trabeculectomy on all patients (N = 85), 37 (49 eyes) of whom received a collagen matrix implant and 48 (50 eyes) of whom received MMC. The inclusion criteria for patient chart selection included at least 12 months of follow-up data and no prior history of retinal, glaucoma, or other anterior segment surgery, with the exception of prior cataract surgery. Relatively equal demographic data and preoperative characteristics were reported, with the majority of patients having a primary diagnosis of primary openangle glaucoma.

According to the investigators, there was a comparable decrease (P = .34) in mean IOP from preoperative levels in the MMC (24.98 decreasing to 12.1 mm Hg) and implant groups (23.24 decreasing to 13.12 mm Hg). High rates of surgical success were noted in the unqualified group (patients on no medications 1 year postoperatively), with an IOP of 21 mm Hg or lower in 84% and 86% of patients in the MMC and implant groups, respectively. Sixty percent of the MMC group and 55% of the implant group achieved an IOP of 13 mm Hg or lower. Qualified successes (patients on glaucoma medications 1 year postoperatively) revealed no statistically significant differences between the two groups. Additionally, there was no statistically significant difference between the groups in the mean number of postoperative medications required (MMC group, 3.04 decreasing to 0.18; implant group, 2.7 decreasing to 0.15).

Overall, complications were similar in both groups,

with identical rates of transient postoperative wound leaks and choroidal effusions. One patient in the MMC group proceeded to no light perception vision after a suprachoroidal hemorrhage. Reoperations included three in the implant group (2 bleb needlings and 1 revision of the Ex-Press device's tip) and seven in the MMC group (3 bleb revisions for leak/hypotony, 1 choroidal drainage, 2 cataract surgeries, and 1 laser trabeculoplasty). Differences in visual acuity remained statistically insignificant between both groups pre- and postoperatively.

DISCUSSION

Bleb leaks and postoperative infection associated with trabeculectomy pose a significant risk in the battle to preserve sight, with the former's being reported at a rate as high as 3.2% per patient year.² The need for improved and adjunct wound-modifying options is a major factor in the long-term control of IOP and visual acuity of glaucoma surgical patients.

According to the authors, the use of the Ologen implant has led to small modifications in the surgical procedure of trabeculectomy, potentially creating a new and feasible alternative to antimetabolite treatments and to the success of glaucoma surgeries. The collagen matrix is an FDA-approved, porcine-derived collagen matrix implant that biodegrades in approximately 90 days. The implant, which has been studied as an adjunct to trabeculectomy in rabbits, is typically fashioned between external scleral and internal Tenon capsule once the scleral flap has been sutured to create the desired flow rate of the sclerostomy. Ologen theoretically serves as a reservoir, with a reported reduction in the number of myofibroblasts demonstrating an irregular scaffolding adherence pattern. This reservoir potentially promotes favorable wound healing with adequately maintained IOP after bleb surgery in lieu of antimetabolite usage.^{3,4}

Earlier studies evaluating the use of the collagen matrix have reported mixed results, with the implant's failing to achieve an IOP-lowering effect similar to that after treatment with MMC.^{5,6} The need for more frequent blebneedling procedures with combined phacotrabeculectomy has also been reported.⁷ The authors of this study make a case for equal efficacy in terms of 12-month measurements of IOP with relatively few complications in both groups. Although the limitations of a single-surgeon, retrospective study mean potential weaknesses in the analysis of data, the opportunity for one operator to optimize his or her surgical technique and report his or her findings can broaden glaucoma surgeons' scope of practice regarding patient management and surgical selection. The availability of these tools can foster our ability to preserve the integrity of postoperative wounds, improve long-term IOP maintenance, and maximize quality years of vision for patients.

SECONDARY SUBCONJUNCTIVAL IMPLANTATION OF A BIODEGRADABLE COLLAGEN-GLYCOSAMINOGLYCAN MATRIX TO TREAT OCULAR HYPOTONY FOLLOWING TRABECULECTOMY WITH MITOMYCIN C

Dietlein TS, Lappas A, Rosentreter A⁸

ABSTRACT SUMMARY

Dietlein et al⁸ present a consecutive case series of 12 eyes in which a biodegradable collagen matrix implant (Ologen) was used as a secondary implant for the treatment of symptomatic ocular hypotony after filtration surgery with MMC.

Twelve glaucoma patients with postoperative hypotony (IOP < 8 mm Hg with choroidal detachment and/or choroidal folds) presenting between 1 and 72 months (mean time, 4.5 months) were treated with secondary implantation of the collagen matrix implant. Two of the 12 patients were noted to have leaking blebs; these blebs were described as thin and avascular. All patients presented with decreased visual acuity compared with preoperative measurements.

Secondary implantations were performed in a controlled and systematic fashion with subconjunctival anesthesia and a temporal approach to the bleb. Depending on the surgeon's determination of bleb morphology, either a 6- by 2-mm or 12- by 1-mm collagen matrix implant was placed over the scleral flap in the subconjunctival space, and the surgical site was closed with an 8–0 Vicryl suture (Ethicon, Inc.). Postoperative treatment consisted of topical steroids and antibiotics.

The authors reported a mean preoperative IOP of 4.4 mm Hg with a statistically significant increase to 9.9 mm Hg at 18 months' follow-up (P < .0001). A significant improvement in visual acuity was seen in nine of the 12 eyes, with no change in three (P = .0012).

Complications included persistent massive choroidal detachment despite an increase in IOP to 11 mm Hg with the implant; an exposed implant requiring repositioning, resulting in resolution of hypotony and a previ"In this case series, the collagen matrix is presented as an additional successful tool in a surgeon's repertoire for battling posttrabeculectomy hypotony associated with MMC use."

ous bleb leak; and corneal dellen treated with artificial tears. Two patients required glaucoma medication 18 months postoperatively to maintain adequate tension control.

DISCUSSION

The introduction of antimetabolites has enhanced the long-term efficacy of trabeculectomy surgery, and the agents' use has remained the standard for preventing the most common causes of failure in incisional glaucoma surgery: fibrosis and scarring.⁹⁻¹¹ Antimetabolites can also create clinical problems, however, ranging from minor bleb leaks to vision-threatening endophthalmitis.

Ocular hypotony falls within the spectrum of complications that presents a frustrating postoperative course for both the patient and the surgeon. Hypotony after glaucoma filtration surgery has traditionally been managed by methods to temporarily increase intraocular tension, either by decreasing overfiltration or by hastening wound healing. Surgical interventions have included viscoelastic injection, autologous blood injection, flap resuturing, conjunctival compression sutures, or preserved pericardium patch grafting.¹² These techniques often require one or more re-attempts to adequately control filtering and can produce devastating IOP spikes.

Secondary implantation of a collagen matrix implant in this case series addresses postsurgical hypotony by increasing outflow resistance through the decrease of aqueous flow and by creating an environment where scaffolding promotes controlled resistance to wound healing within the sub-Tenon space. Histopathology section of exposed, superficial collagen matrix in a single patient from this case series revealed myofibroblasts surrounding and invading the glycosaminoglycan scaffolding, as demonstrated in animal models and in support of intrableb observational wound healing.^{13,14}

Potential advances from the use of a collagen matrix implant address classic complications of trabeculectomy surgery with adjunctive MMC and include promoting increased vascularization in avascular, cystic blebs; reducing contractile shrinkage within a bleb; and decreasing the fluctuation of IOP peaks after implantation of the matrix. In this case series, the collagen matrix is presented as an additional successful tool in a surgeon's repertoire for battling posttrabeculectomy hypotony associated with MMC use. Further studies are warranted to determine the long-term efficacy of the collagen matrix and other glycosaminoglycan implants. Surgeons should re-evaluate patients at each visit for the risk of bleb fibrosis and create customized management plans to promote the best functional and visual outcomes. The effects of implanting materials in the subconjunctival space should continue to be individualized pending further research on the complexity of wound healing.

Section Editor James C. Tsai, MD, is the Robert R. Young professor of ophthalmology and visual science and the chair of the Department of Ophthalmology & Visual Science at Yale School of Medicine in New Haven, Connecticut. Dr. Tsai may be reached at (203) 785-2020; james.tsai@yale.edu.

Sarah Khodadadeh, MD, is a clinical instructor and glaucoma fellow at Yale University/ Yale Eye Center in New Haven, Connecticut. She acknowledged no financial interest in the products or companies mentioned herein.



Dr. Khodadadeh may be reached at (203) 785-2020; sarah.khodadadeh@yale.edu.

1. Johnson MS, Sarkisian SR Jr. Using a collagen implant (Ologen) versus mitomycin-C as a wound healing modulator in trabeculectomy with the Ex-Press mini glaucoma device: a 12-month retrospective review [published online ahead of print November 14, 2013]. *J Glaucoma*. doi:10.1097/J/JG.000000000000018.

2. Debry PW, Perkins TW, Heatly G, et al. Incidence of late-onset bleb-related complications following trabeculectomy with mitomycin. Arch Ophthalmol. 2002;120:297–300.

 Chen HS, Ritch R, Krupin T, et al. Control of filtering bleb structure through tissue bioengineering: an animal model. Invest Ophthalmol Vis Sci. 2006;47:5310-5314.

4. Hsu WC, Ritch R, Krupin T, et al. Tissue bioengineering for surgical bleb defects: an animal study. *Graefes Arch Clin Exp Ophthalmol.* 2008;246:709-717.

5. Rosentreter A, Schild AM, Jordan JF, et al. A prospective randomized trial of trabeculectomy using mitomycin C vs an Ologen implant in open angle glaucoma. *Eye*. 2010;24:1449-1457.

6. Boey PY, Narayanaswamy A, Aheng C, et al. Imaging of blebs after phacotrabeculectomy with Ologen collagen matrix implants. *Br J Ophthalmol.* 2011;95:340-344.

 Narayanaswamy A, Perera SA, Htoon HM, et al. Efficacy and safety of collagen matrix implants in phacotrabeculectomy and comparison with mitomycin C augmented phacotrabeculectomy at 1 year. *Clin Experiment Ophthalmol.* 2013;41(6):552–560.

 Dietlein TS, Lapas A, Rosentreter A. Secondary subconjunctival implantation of a biodegradable collagenglycosaminoglycan matrix to treat ocular hypotony following trabeculectomy with mitomycin C. Br J Ophthalmol. 2013;97(8):985–988.

9. Khaw PT, Doyle JW, Sherwood MB, et al. Prolonged localized tissue effects from 5-minute exposures to 5-fluorouracil and mitomycin C. Arch Ophthalmol. 1993;111:263-267.

10. Cordeiro MF, Reichel MB, Gay JA, et al. Transforming growth factor-beta 1, -beta 2, and -beta 3 in vivo: effects on normal and mitomycin C-modulated conjunctival scarring. *Invest Ophthalmol Vis Sci*. 1999;40:1975–1982.

11. Hitchings RA, Grierson I. Clinico pathological correlation in eyes with failed fistulising surgery. *Trans Ophthalmol Soc UK*. 1983;103:84–88.

12. Allingham RR, Damji K, Freedman S, et al. *Shields' Textbook of Glaucoma*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:568-609.

13. Peng YJ, Pan CY, Hsieh YT, et al. The application of tissue engineering in reversing mitomycin C-induced ischemic conjunctiva. *J Biomed Mater Res Part A*. 2012;100A:1126–1135.

14. Min JK, Kee CW, Sohn SW, et al. Surgical outcome of mitomycin C-soaked collagen matrix implant trabeculectomy. J Glaucama. 2013;22(6):456–462.