Modified Trabeculectomy Using Ologen® Collagen Matrix with or without A Cyclodestructive Procedure for Canine Glaucoma: A Retrospective Review of 14 Cases

Sung-Jun Lee¹ Joon-Young Kim^{2,†} Soon-wuk Jeong¹

¹Department of Veterinary Surgery, College of Veterinary Medicine, Konkuk University, 120 Neungdong-ro, Gwangjin-gu, Seoul, Korea

²Veterinary Medical Teaching Hospital, Konkuk University, 120 Neungdong-ro, Gwangjin-gu, Seoul, Korea

[†]Corresponding author: Joon-Young Kim
Veterinary Medical Teaching Hospital, Konkuk University,
120 Neungdong-ro, Gwangjin-gu, Seoul, 05029, Republic of Korea
Tel.: 82-2-444-6150
Fax: 82-2-444-4396
E-mail: canvet@hanafos.com

KEY WORDS: canine glaucoma, cyclodestructive procedure, filtering surgery, intraocular pressure, ologen® CM, trabeculectomy

ABSTRACT

Trabeculectomy in the dogs has not generally used because of filtering bleb failure due to episcleral fibrosis and subconjunctival scarring for glaucoma. To overcome this filtering bleb failure, we applied a modified trabeculectomy using ologen® Collagen Matrix (CM) with or without a cyclodestructive procedure for dogs with medically uncontrolled glaucoma. This study was performed as retrospective case series. 14 eyes of 12 dogs with medically uncontrolled glaucoma was evaluated from 2015 through 2016. The dogs were divided into three groups: group 1 (six eyes), modified trabeculectomy using ologen® CM (MTO); group 2 (four eyes), MTO with transscleral cyclo-

Intern J Appl Res Vet Med • Vol. 17, No. 2, 2019.

photocoagulation (TSCP); and group 3 (four eves), MTO with endocyclophotocoagulation (ECP). Data pertaining to signalment, pre- and postoperative intraocular pressure (IOP) and visual acuity, preoperative management, detailed surgical procedures, postoperative treatments, follow-up duration, surgical outcomes, and complications were retrospectively reviewed. The outcomes of trabeculectomy and bleb formation were evaluated using ultrasound biomicroscopy (UBM). IOP was successfully stabilized at < 25 mmHg at different time points in 12 of the 14 (85.7%) eyes. Six of nine eyes (66.7%) maintained vision after surgery, and two of five (40.0%) eyes with preoperative vision loss regained vision after surgery. All eyes except two exhibited successful filtering bleb formation without major complications. IOP showed no significant differences among groups (P > 0.05). Modified trabeculectomy using ologen® CM is easy to perform and demonstrates successful outcomes with minimal postoperative complications. This new surgical technique may be an effective alternative procedure for IOP control in canine glaucoma.

INTRODUCTION

Glaucoma is one of the common causes of vision loss in humans and animals.1,2 Currently, transscleral cyclophotocoagulation (TSCP), and endocyclophotocoagulation (ECP) and are considered effective methods for lowering IOP in animals.^{3,4} But ECP is generally performed at the time of phacoemulsification with intraocular lens implantation to prevent postoperative secondary cataract formation.5 And TSCP can cause short- and long-term complications, such as postoperative intraocular hypertension, hyphema, uveitis, secondary cataract, and ulcerative keratitis.⁴ In the field of veterinary ophthalmology, the most common filtering procedures involve the use of anterior chamber shunts or gonioimplantation.6 Several reports have described gonioimplantation as an effective procedure for normalizing IOP and maintaining vision in dogs with medically uncontrolled glaucoma.^{2,7,8,9} However, it is associated with early and late complications, including hypotony, anterior uveitis, tube obstruction, conjunctival erosion, tube migration, corneal endothelial decompensation, and filtering bleb failure, in humans and dogs.^{6,10} Trabeculectomy which is another filtering surgery has not generally used because of filtering bleb failure due to episcleral fibrosis and subconjunctival scarring for glaucoma in the dogs.4,6 Excessive fibrosis of the filtering bleb may lead to bleb failure and lower the success rate of filtering surgeries, including trabeculectomy and gonioimplantation, in both humans and animals.^{11,12} To prevent bleb scarring, several adjunctive antimetabolies, including mitomycin C (MMC) and 5-fluorouracil (5-FU), are commonly used.^{2,11,13} Although the use of antimetabolites during or following surgery has improved the long-term success rate for filtering surgeries,^{2,8} it has increased the rate

of bleb-related complications such as bleb leakage, subconjunctival tissue necrosis, hypotony maculopathy, blebitis, and endophthalmitis.^{2,7} Recently, tissue-engineered implants were developed as alternatives to MMC and 5-FU, with lesser adverse effects. One of these is the ologen® Collagen Matrix (ologen® CM, Aeon, Astron, Leiden, the Netherlands), which consists of lyophilized porcine atelocollagen and glycosaminoglycan with a 10- to 300-µm pore size. It is biodegradable and an implantable extracellular matrix (ECM) mimic specifically configured to support and modulate tissue repair processes in connective and epithelial ocular tissues.14 According to recently reported studies on glaucoma filtering surgeries performed in animal models and humans, ologen® CM is effective in promoting bleb formation by modulating fibroblast migration and proliferation into the pore structures and normalizing secreted collagen and another extracellular matrix deposition, resulting in reduced scar formation.^{15,16} In the present study, we aimed to determine a surgical technique that is easier and less complicated than gonioimplantation, which is the most commonly used method, and in our opinion, the use of ologen® CM for trabeculectomy may be an effective alternative for the surgical treatment of canine glaucoma. Although, to the best of our knowledge, no previous study has documented the outcomes of modified trabeculectomy using ologen® CM with or without a cyclodestructive procedure for the treatment of canine glaucoma. The aim of the present study was to describe the surgical techniques and clinical outcomes associated with modified trabeculectomy using ologen® CM with or without a cyclodestructive procedure for medically uncontrolled glaucoma in 12 dogs (14 eyes).

MATERIALS AND METHODS Review of medical records

The medical records at Veterinary Medical Teaching Hospital (VMTH), Konkuk University were reviewed to identify 14 eyes of 12 dogs with medically uncontrolled **Figure 1.** Modified trabeculectomy with ologen® Collagen Matrix (CM) for medically uncontrolled glaucoma in dogs. (a) A fornix-based conjunctival/ Tenon's flap is prepared at the 12 o'clock position, 0.5 mm behind the superior limbus. (b) A rectangular 2.0 x 2.0-mm2 wide, 300-µm thick limbal-based scleral flap is dissected using a crescent knife.

(c) A 1 to 1.5-mm trabeculectomy window is created using a corneoscleral punch for glaucoma after the placement of a stab incision using a No. 11 blade. (d) The scleral flap is repositioned with ologen® CM (8.0 $\times 2.0 \times 2.0$ mm) implanted beneath it. (e) Flap closure is achieved with two interrupted sutures, one tight and one loose, using 10-0 nylon on the bilateral edges of the flap. (f) Another ologen® CM (10.0 \times 8.0 \times 2.0 mm) implant is positioned over the scleral flap without the use of sutures. (g) The conjunctiva is closed with a simple continuous suture pattern using 9-0 polyglactin 910.



glaucoma treated by modified trabeculectomy using ologen® CM with or without a cyclodestructive procedure (TSCP or ECP) from 2015 through 2016. Data pertaining to signalment, pre- and postoperative IOP and visual acuity, preoperative management, detailed surgical procedures, postoperative treatment, follow-up duration, surgical outcomes, and postoperative complications were collected. The outcomes of trabeculectomy and bleb formation were also evaluated using ultrasound biomicroscopy (UBM). All eyes were divided into three groups according to the surgical procedure. Six eyes (cases 1–6, group 1) underwent modified trabeculectomy using ologen® CM (MTO), four eyes (cases 7–10, group 2) underwent MTO with TSCP, and four eyes (cases 11–14, group 3) underwent MTO with ECP. Pre- and postoperative IOP was evaluated using applantation tonometry (Tonopen VetTM, Reichert. INC., Depew, NY, USA). All data were statistically analyzed using SPSS statistics 24.0 for Windows (IBM, Armonk, NY, USA). The normality of data distribution was evaluated using the Shapiro-Wilk test. One-way ANOVA and the Kruskal-Wallis test were performed to compare differences in mean IOP values at different time points (before surgery; 5 h, 1 day, and 1, 2, 3, 4, 5, 6, and 12 months after surgery) among the three groups. A P-value of <0.05 was considered statistically significant.

Modified trabeculectomy using ologen® CM

General anesthesia was induced with intravenous propofol (6 mg/ kg; Provive 1%, Myungmoon Pharm. Co., Ltd, Korea) and maintained with 1.5%–2.0 % isoflurane

Complications	None	None	Fibrin deposition	None	None	Corneal edema	None	Uveitis, Corneal ulceration,	None	Uveitis Hyphema	None	Uncontrolled IOP	Uveitis, Corneal edema	None
Maintenance of IOP below 20 mmHg during the follow-up period	0	0	0	0	0	0	0	Х	0	0	0	х	0	0 lle. PACG: primary anele-closure elaucoma, MTC
Follow-up duration (weeks)	52	26	26	56	13	10	22	54	23	70	53	14	52	42 Tzu. MP: Miniature Pooa
Post-OP visual status	52	26	26	56	13	10	22	54	23	70	53	14	52	42 ter Spaniel. ST: Shih
Post-OP visual status	Vision maintained	Vision maintained	Vision maintained	Blind	Vision maintained	Vision maintained	Vision maintained	Blind ^a	Vision maintained	Blind	Vision maintained	Blind ^b	Blind	Blind ^e 1. ECS: English Coch
Pre-OP visual status	Vision maintained	Blind	Vision maintained	Blind	Vision maintained	Vision maintained	Vision maintained	Vision maintained	Blind	Blind	Vision maintained	Vision maintained	Blind	Vision maintained erican Cocker Spanie
Surgery	MTO	MTO	MTO	MTO	MTO	MTO	MTO, TSCP	MTO, TSCP	MTO, TSCP	MTO, TSCP	MTO, ECP	MTO, ECP	MTO, ECP	MTO, ECP
Pre-OP IOP	41	35	35	42	41	40	39	38	56	50	40	45	45	32 itraocular pre
Cause of glaucoma	Cataract surgery	PACG	Chronic uveitis	Chronic uveitis	Cataract surgery	Cataract surgery	PACG	Chronic uveitis	Chronic uveitis	Chronic uveitis	Cataract surgery	Cataract surgery	Cataract surgery	Cataract surgery
Age	ε	12	Ś	14	S	4	10	10	11	10	б	4	б	9 -OP: noste
Breed	ACS	ECS	ST	MP	ACS	ECS	ECS	ST	ST	ST	ACS	ACS	MP	Samoyed
Case No.	-	7	б	4	Ś	9	٢	8	6	10	11	12	13	14 <i>re-OP: pr</i>

and in each case June 1.1.1 ad aliminal data of anoinal an -£ (Isoflurane; Choongwae Co., Ltd, Korea). Normal saline 0.9% was used for intraoperative fluid management. The dog was positioned in dorsal recumbency, and the affected eye was clipped and prepared for surgery using 0.2% povidone-iodine solution for sterilization of the ocular surface. For adequate globe positioning, intravenous atracurium besylate (0.2 mg/kg; Atra®, Hana pharm Co., Ltd., Seoul, Korea) was administered just before surgery. All 14 eyes underwent trabeculectomy using the same procedure. A fornix-based conjunctival/ Tenon's flap positioned at 12 o'clock was prepared by dissection of the conjunctiva and Tenon's capsule 0.5 mm behind the superior limbus using Westcott tenotomy scissors (Fig. 1a). A rectangular 2.0×2.0 -mm2, 300-µm thick limbal-based scleral flap was dissected using a crescent knife (Fig. 1b), and a 1 to 1.5-mm trabeculectomy window was created using a corneoscleral punch for glaucoma after the placement of a stab incision using a No. 11 blade (Fig. 1c). The scleral flap was repositioned with ologen® CM ($8.0 \times 2.0 \times 2.0$ mm) implanted beneath it (Fig. 1d). Flap closure was achieved with two interrupted sutures, one tight and one loose, using 10-0 nylon (ALCON® Closure Systems, Alcon Laboratories, Inc. Texas, USA) on the bilateral edges of the flap (Fig. 1e). Another ologen \mathbb{R} CM (10.0 \times 8.0 \times 2.0 mm) implant was positioned over the scleral flap without the use of sutures (Fig. 1f). Finally, the conjunctiva was closed with a simple continuous suture pattern using 9-0 polyglactin 910 (Vicryl*, Ethicon LLC, USA) (Fig. 1g). An intracameral injection of tissue plasminogen activator (tPA, 25 µg; Actilase[®], Beringer Ingelheim, Germany) was administered after surgery. **Cyclodestructive procedure**

TSCP using a diode laser (Diovet, Iris Medical Instruments, Mountain View, CA, USA) was performed before trabeculectomy in four dogs. Energy was delivered to 20 sites by 600-µm spots with a power setting of 1000 mV for a duration of 5000 ms. The 12 o'clock site was avoided in order to perform trabeculectomy.

ECP using a diode laser (Diovet, Iris Medical Instruments, Mountain View, CA, USA) with the E4 Ophthalmic Laser Endoscopy system (Endo Optiks Little Silver, New Jersey, USA) was performed before trabeculectomy in four dogs with pseudophakia. Ciliary process ablation using 250 mV was performed within a range of 180° to 270°. Whitening and contraction of each treated ciliary process were identified.

Postoperative management

After the surgery in each animal, prednisolone acetate 1% (Pred Forte®, Allergan, Inc., Irvine, CA) and ofloxacin (Tarivid®, Santen Pharm., Ltd, Korea) were topically applied on the operated eye every 6 h. Over a duration of 2 to 4 weeks, ofloxacin was discontinued if there was no evidence of infectious disease. The frequency of prednisolone acetate 1% was gradually tapered, with a maintenance frequency of once a day. The frequency and number of antiglaucoma medications were gradually decreased with a decrease in or normalization of IOP.

RESULTS

In total, there were three English Cocker Spaniels (three eyes), three American Cocker Spaniels (four eyes), three Shih Tzus (four eyes), two Miniature Poodles (two eyes), and a Samoyed (one eye). The mean age was 8.5 years (range, 3–14 years). All eyes were diagnosed with glaucoma: five with glaucoma secondary to chronic uveitis, seven with glaucoma as a complication of cataract surgery, and two with primary angle-closure glaucoma (PACG). All eyes exhibited intraocular hypertension (IOP > 25 mmHg) before surgery despite antiglaucoma medications such as β -adrenoceptor blockers, α 2-adrenoceptor agonist, carbonic anhydrase inhibitor, and prostaglandin analogs. The clinical data for all eyes are shown in Table 1. Following surgery, IOP was successfully stabilized at <20 mmHg at different time points in 12 of the 14 eyes (cases 1-7, 9-11, 13, 14; 85.7%). The antiglaucoma medications for these 12 eyes were gradually tapered or discontinued

Day	Group 1 (<i>n</i> -6)	Group 2 (n = 4)	Group 3 (n = 4)	P-value
Pre-OP	39.00 ± 3.16	45.75 ± 8.73	40.50 ± 6.14	0.629ª
Post-OP	12.17 ± 2.48	26.50 ± 13.03	23.00 ± 11.23	0.063ª
1 day	13.67 ± 1.97	20.00 ± 7.26	29.50 ± 15.42	0.130ª
1 month	15.17 ± 7.60	17.75 ± 7.27	24.00 ± 11.97	0.235ª
2 months	16.17 ± 6.61	13.50 ± 4.04	19.67 ± 13.32 (n = 3)	0.608 ^b
3 months	15.00 ± 3.74 (n = 5)	14.50 ± 4.80	14.00 ± 1.00 (n = 3)	0.935 ^b
4 months	14.50 ± 3.70 (n = 4)	14.50 ± 3.70	14.00 ± 1.00 (n = 3)	0.919 ^b
5 months	13.75 ± 1.89 (n = 4)	16.00 ± 5.03	14.00 ± 1.73 (n = 3)	0.717ª
6 months	12.75 ± 2.22 (n = 4)	15.33 ± 5.77 (n = 3)	13.67 ± 2.08 (n = 3)	0.841ª
12 months	12.50 ± 3.54 (n = 2)	17.50 ± 10.60 (n = 2)	15.50 ± 2.12 (n = 2)	c

Table 2. Evaluation of IOP (mean \pm SD) values during the follow-up period for each group.

Group 1: modified trabeculectomy using ologen® CM (MTO), Group 2: MTO with trans-scleral cyclophotocoagulation, Goup 3: MTO with endocyclophotocoagulation, Pre-OP: preoperative, Post-OP: 5 h after surgery, aKruskal– Wallis test, bOne-way ANOVA, cStatistical verification not possible because of small sample size

on the basis of IOP normalization. Although IOP exhibited a transient increase (>25 mmHg) in seven (cases 1, 4, 5, 6, 11, 13, 14) of the 12 eves between 1 day and 41 weeks (mean, 9.9 weeks; median, 6 weeks) after surgery, it normalized immediately or within a few days after the temporary administration of antiglaucoma and anti-inflammatory medications with or without tPA injections in the anterior chamber. The number of antiglaucoma medications required by these 12 eyes was smaller after surgery than before surgery. Postoperative hypotony was not observed in any eye. In the remaining 2 eyes (cases 8 and 12), however, IOP could not be effectively controlled after surgery. Case 12 demonstrated intraocular hypertension immediately after surgery, and IOP could not be controlled despite intensive medical treatment and anterior chamber paracentesis. This eye lost vision within a day after surgery and exhibited a persistently elevated IOP for 14 weeks. Eventually, it was eviscerated. Case 8 exhibited an elevated IOP at 1 week after surgery. Slit-lamp examination revealed deep corneal ulceration with severe uveitis, and the eye lost vision despite medical treatment. The corneal ulcer and uveitis recovered after 1 month of intensive medical treatment, although severe fluctuations in IOP were observed (from 10 mmHg to 41 mmHg). At the time of glaucoma surgery, nine eyes (cases 1, 3, 5-8, 11, 12, 14) exhibited intact visual function; this was maintained in six eyes (cases 1, 3, 5-7, 11; 66.7%) after surgery. The remaining three eyes (cases 8, 12, 14) lost vision within 1 day to 231 days (mean, 80 days) after surgery. Cases 8 and 12 lost vision because of uncontrolled high IOP, as explained above. Case 14 exhibited a transient IOP increase and vision loss at 41 weeks after surgery. Before this, the condition of the eyes was very good with no other side effects and well-maintained vision, which was lost despite IOP normalization. This dog died 3

months later because of diabetic complications. Finally, two (cases 2, 9; 40%) of five eyes (cases 2, 4, 9, 10, 13) with preoperative blindness regained vision within 1 day after surgery.

Slit-lamp biomicroscopy and UBM examinations revealed the successful formation of filtering blebs without major complications, including conjunctival necrosis or dehiscence and endophthalmitis, during the follow-up period for all eyes except two (cases 8, 12), which did not achieve effective IOP control. Ologen® CM was gradually resorbed, and a clear drainway for aqueous humor from the anterior chamber was detected around the scleral flap on UBM examinations (Fig. 2). Mild conjunctival hyperemia around the bleb, which resolved with short-term anti-inflammatory treatment, was occasionally observed in three eyes (cases 1, 9, 11). IOP normalized immediately after surgery and was satisfactorily maintained over the long-term follow-up period. There were no significant differences

Figure 2. Evaluation of bleb formation using ultrasound biomicroscopy after modified trabeculectomy using ologen® Collagen Matrix (CM) for medically uncontrolled glaucoma in dogs. Ologen® CM is gradually resorbed, and a clear drainway for aqueous humor from the anterior chamber is visible around the scleral flap. (A) Four days after surgery (case 2), (B) 10 days after surgery (case 7), (C) 26 days after surgery (case 6), (D) 90 days after surgery (case 4), (E) 100 days after surgery (case 1), (F) 150 days after surgery (case 11), H: 1–1.5mm trabeculectomy window, SF: scleral flap, B: bleb, D: drainway under the scleral flap



Intern J Appl Res Vet Med • Vol. 17, No. 2, 2019.

in IOP values at different time points among the three groups (P > 0.05; Table 2).

DISCUSSION

In the present study, we demonstrated a new filtering surgery involving modified trabeculectomy using ologen® CM with or without a cyclodestructive procedure (ECP or TSCP) for IOP control and vision maintenance in dogs with medically uncontrolled glaucoma. IOP was controlled in 12 of the 14 included eyes (85.7%). Six of nine eyes (66.7%) with intact vision before surgery maintained their vision after surgery, and two of five eyes (40%) with preoperative blindness regained vision. Our success rates for IOP control and vision maintenance after surgery are comparable with those previously reported for glaucoma drainage device (GDD) implantation (75% and 66.7%, respectively),8 gonioimplantation (76%/46%) with TSCP,7 and trabeculectomy with or without TSCP $(55.6\%/66.7\%)^{17}$ in studies with varying follow-up periods. Currently, the placement of an anterior chamber shunt, such as an Ahmed valve, a Baerveldt drainage implant, and a Krupin-Denver valve, Cullen frontal sinus valved glaucoma shunt, using gonioimplantation has been considered the most common filtering procedure for medically uncontrolled glaucoma in animals,^{1,4,6,18} and several studies have reported successful outcomes of this procedure for medically uncontrolled glaucoma in dogs.2,7,8,16 However, in humans, trabeculectomy is a common surgical procedure for the treatment of uncontrolled glaucoma. According to many studies focusing on a comparison of longterm outcomes between gonioimplantation and trabeculectomy for glaucoma, there is no difference between the two procedures.¹⁹ However, Tran et al reported that trabeculectomy is more effective than gonioimplantation for lowering IOP.²⁰ The advantages of trabeculectomy include the lack of complications caused by intraocular implants, such as tube occlusion and migration, irritation of the corneal endothelium, tissue necrosis around the reservoir base, implant exposure, and chronic anterior uveitis with a longterm foreign body reaction due to nonbiodegradable devices.20 Trabeculectomy is a surgical method for the stabilization of IOP by draining aqueous humor from anterior chamber to the space between the sclera and the conjunctiva. After ocular tissue damage caused by surgical procedure, normal wound healing reaction occurs in the body. The wound healing process is a complex physiological mechanism for tissue repair including coagulation, inflammation, fibroplasia, angiogenesis, epithelization, maturation, and remodeling. After the acute inflammatory response, fibroblasts migrate and proliferate into the wound site by growth factors included transforming growth factor-B $(TGF-\beta)$ and platelet-derived growth factor (PDGF) which are released by macrophages and platelets. Fibroblasts, play a key role in the formation of scar tissue, synthesize new collagen and other extracellular matrix that are important components of granulation tissue. Deposition and organization of newly synthesized collagen in the parallel to the fibroblasts which are oriented in the wound bed. Unidirectional alignment of collagen provides tensile strength of the scar tissue, and it is different from aligned randomly collagen in normal connective tissue.21 Filtering bleb failure due to episcleral fibrosis and subconjunctival scarring is the major cause of poor outcomes after filtering surgery for glaucoma in animals.^{4,6} For the prevention of excessive scar tissue formation, antimetabolites, such as MMC and 5-FU, are widely used in human and dogs during or after glaucoma filtering surgery. These agents are useful in inhibition of fibroblast growth and replication, however, they can cause severe complications associated with their widespread fibroblast cytotoxicity and apotosis, including conjunctival necrosis, thin-walled avascular bleb formation, bleb leakage, bleb-related infection, and endophthalimits.^{6,21} Recently, as alternatives to antimetabolites, biodegradable collagen materials such as ologen® CM were introduced for use in trabeculectomy and other glaucoma filtering procedures.¹⁶ This implant is composed of three-dimensional, porous,

collagen-glycosaminoglycan copolymers that can encourage fibroblasts and myofibroblasts to grow in to the matrix pores and secrete connective tissue in the form a loose matrix. By guiding the pattern of cellular migration, that should promote random orientation of collagen deposition similar to normal connective tissue, it inhibited the dense scar tissue formation and wound contraction. And also, application of the implant in the space between episclera and conjunctiva can form a mechanical barrier that may prevent adhesion between these two tissue layers during the early postoperative period.^{16,22} In addition, according to a previous experimental study in an animal model, implant-induced pressure created by positioning between the scleral flap and conjunctiva contributes to the prevention of excessive aqueous humor drainage.14 Excessive outflow of aqueous humor with inflammatory mediators into the subconjunctival space in uveitic conditions can lead to increased bleb fibrosis and, consequently, a poor prognosis.² Therefore, the use of ologen® CM aids in the maintenance of adequate bleb function. In the present study, functional blebs were formed in 12 of the 14 eyes (85.7%) at the last follow-up visit. In the present study, we implanted ologen® CM not only subconjunctivally, similar to its placement during conventional glaucoma filtering procedures in humans, but also subsclerally. We believe that the subconjunctival implant aided in the formation of an adequate filtering bleb, while the subscleral implant maintained the surgical passage for aqueous humor outflow through the prevention of subscleral fibrosis. Thus, ologen® CM implantation contributed to the successful control of IOP in our patients. In addition, this technique can prevent early postoperative hypotony, which causes hypotensive retinopathy with multifocal retinal folds because of overfiltration of aqueous humor. It is one of the most common complications of glaucoma filtering surgery in humans and animals.^{2,6,8} Several modified techniques for the prevention of hypotony immediately after trabeculectomy have been studied.23 Suturing the bilateral

edges of the scleral flap is considered an effective method, and very loose or very tight sutures can cause postoperative hypotony or ocular hypertension, respectively. In the present study, we applied one tight and one loose suture on the bilateral edges of the scleral flap to restore it to its original position. Postoperative transient IOP spikes can lead to adverse effects on long-term visual outcomes because of ischemic damage to the optic disc and retina. Early detection of reelevated IOP and efforts for normalization with active treatments, including medications and revision surgery, are important for successful outcomes.^{2,7,8} In this case series, a transient IOP spike, including early postoperative intraocular hypertension, was observed in seven eyes at different time points after surgery, and it resolved with additional anti-inflammatory and antiglaucoma medications in all eyes.

We identified bleb and drainway formation using UBM in our study. In most cases, ologen® CM was completely resorbed at 90 days after surgery. A drainway was detected at approximately 2 weeks, while bleb formation was detected at approximately 1 month after surgery. Postoperative IOP values showed no differences among the three groups in our study, which suggests that the outcomes of trabeculectomy alone and trabeculectomy with a cyclodestructive procedure are not different. However, a transient IOP spike occurred more frequently in the early postoperative period in dogs that underwent trabeculectomy with a cyclodestructive procedure. Several reports on cyclophotocoagulation documented intraocular hypertension within 1 week after surgery as the most common early postoperative complication.^{1,3} Trabeculectomy for secondary glaucoma, particularly that caused by uveitis, is more challenging compared with that for primary glaucoma in humans.¹⁹ Chronic and recurrent intraocular inflammation can result in postoperative hypotony due to ciliary body impairment. Moreover, active intraocular inflammation can promote undesired and excessive scarring of the subconjunctival bleb and adherence of the

scleral flap. The recurrence of uveitis should be prevented by aggressive anti-inflammatory treatments, including intracameral injection of tPA and continuation of topical and/ or systemic steroid application, in order to improve the prognosis after trabeculectomy for secondary glaucoma.

The findings of the present study demonstrate that modified trabeculectomy using ologen® CM with or without a cyclodestructive procedure can control IOP and maintain vision in dogs with medically uncontrolled glaucoma. This modified surgical technique and additional collagen matrix implantation can result in successful outcomes with minimal complications such as postoperative hypotony and bleb fibrosis. However, further studies on methods to control transient IOP spikes after surgery and the optimal position of ologen® CM for minimizing bleb and drainway fibrosis are warranted. To the best of our knowledge, this is the first study on the outcomes of modified trabeculectomy using ologen® CM for medically uncontrolled glaucoma in dogs.

REFERENCES

- Plummer CE., Regnier A, Gelatt KN. 2013. The canine glaucomas, In: Gelatt KN, Gilger BC, Kern TJ, eds. *Veterinary Ophthalmology* 5th ed. Iowa, USA: John Wiley & Sons, Inc; 1050-1145.
- Westermeyer HD, Hendrix DV, Ward DA. 2011. Long-term evaluation of the use of Ahmed gonioimplants in dogs with primary glaucoma: nine cases (2000–2008). J Am Vet Med Assoc 238:610-617.
- Bras D, Maggio F. 2015. Surgical treatment of canine glaucoma: cyclodestructive techniques. *Vet Clin North Am Small Anim Pract* 45:1283-1305.
- Gelatt KN, Esson DW, Plummer CE. 2011. Surgical procedures for the glaucomas. In: Gelatt KN, Gelatt JP, eds. *Veterinary Ophthalmic Surgery. China*, Elsevier Saunders; 265-303.
- Bras ID, Robbin TE, Wyman, Rogers AL. 2005. Diode endoscopic cyclophotocoagulation in canine and feline glaucoma [abastract]. *Vet Ophthalmol* 8:449.
- Maggio F, Bras D. 2015. Surgical treatment of canine glaucoma: Filtering and end-stage glaucoma procedures. *Vet Clin North Am Small Anim Pract* 45:1261-1282.
- Sapienza JS, Van Der Woerdt A. 2005. Combined transscleral diode laser cyclophotocoagulation and Ahmed gonioimplantation in dogs with primary glaucoma: 51 cases (1996–2004). *Vet Ophthalmol* 8:121-127.

- Graham KL, Donaldson D, Billson FA, Billson FM. 2017. Use of a 350-mm2 Baerveldt glaucoma drainage device to maintain vision and control intraocular pressure in dogs with glaucoma: a retrospective study (2013–2016). *Vet Ophthalmol* 20:427-434.
- García-Sánchez GA, Whitley RD, Brooks DE, Trigo F, Piñón A. 2005. Ahmed valve implantation to control intractable glaucoma after phacoemulsification and intraocular lens implantation in a dog. *Vet Ophthalmol* 8:139-144.
- Wilson MR, Mendis U, Paliwal A, Haynatzka V. 2003. Long-term follow-up of primary glaucoma surgery with Ahmed glaucoma valve implant versus trabeculectomy. *Am J Ophthalmol* 136:464-470.
- Ji Q, Qi B, Liu L, Guo X, Zhong J. 2015. Efficacy and safety of Ologen implant versus mitomycin C in primary trabeculectomy: a meta-analysis of randomized clinical trials. J Glaucoma 24:e88-e94.
- 12. Tinsley DM, Betts DM. 1994. Clinical experience with a glaucoma drainage device in dogs. *Vet Comp Ophthalmol* 4:77-84.
- WuDunn D, Cantor LB, Palanca-Capistrano AM, Hoop J, Alvi NP, Finley C, Lakhani V, Burnstein A, Knotts SL. 2002. A prospective randomized trial comparing intraoperative 5-fluorouracil vs mitomycin C in primary trabeculectomy. *Am J Ophthalmol* 134:521-528.
- Chen HS-L, Ritch R, Krupin T. Hsu W-C. 2006. Control of filtering bleb structure through tissue bioengineering: an animal model. *Invest Ophthalmol ViSI Sci* 47:5310-5314.
- Angmo D, Wadhwani M, Upadhyay AD, Temkar S, Dada T. 2017. Outcomes of trabeculectomy augmented with subconjunctival and subscleral Ologen implantation in primary advanced glaucoma. *J glaucoma* 26:8-14.
- Park KH, Kim JY, Choo SW, Yoon HY, Jeong SW. 2016. Ahmed glaucoma valve implantation with Ologen® Collagen Matrix for the surgical treatment of feline glaucoma. *Vet Ophthalmol* 96-100.
- Amagai Y, Karasawa K, Matsuda H, Tanaka A. 2014. Diode laser transscleral cyclophotocoagulation in combination with trabeculectomy for surgical therapy of canine refractory glaucoma. J Vet Med Res 1:1010.
- Cullen CL. 2044. Cullen frontal sinus valved glaucoma shunt: preliminary findings in dogs with primary glaucoma. *Vet Ophthalmol* 7:311-318.
- Kwon HJ, Kong YXG, Tao LW, Lim LL, Martin KR, Green C, Ruddle J, Crowston JG. 2017. Surgical outcomes of trabeculectomy and glaucoma drainage implant for uveitic glaucoma and relationship with uveitis activity. *Clinl Exp Ophthalmol* 2017.
- Tran DH, Souza C, Ang MJ, Loman J, Law SK, Coleman AL, Caprioli J. 2009. Comparison of long-term surgical success of Ahmed valve implant versus trabeculectomy in open-angle glaucoma. *Br J Ophthalmol* 93:1504-1509.

- Lama PJ, Fechtner RD. 2003. Antifibrotics and wound healing in glaucoma surgery. Surv Ophthalmol 48:314-346.
- Hsu W-C, Spilker MH, Yannas IV, Rubin PA. 2000. Inhibition of conjunctival scarring and contraction by a porous collagen-glycosaminoglycan implant. *Invest Ophthalmol Vis Sci* 41:2404-2411.
- 23. Laspas P, Culmann PD, Grus FH, Prokosch-Willing V, Poplawksi A, Pfeiffer N, Hoffmann EM. 2016. A new method for revision of encapsulated blebs after trabeculectomy: combination of standard bleb needling with transconjunctival scleral flap sutures prevents early postoperative hypotony. *PloS One* 11:e0157320.