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REVIEW

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A review of glaucoma surgical therapy

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Abstract

Glaucoma is a disorder of all species due to a rise of intraocular pressure (IOP) beyond which is compatible with ganglion cell and axon function, often resulting in optic nerve degeneration and irreversible blindness. Glaucoma treatment with surgical intervention aimed at either reducing aqueous production, or increasing or altering aqueous outflow has evolved over preceding decades, but there remains no cure. The present article is intended to provide a concise review of glaucoma surgical therapies in veterinary ophthalmology.

KEYWORDS

endolaser cyclophotocoagulation, glaucoma, gonioimplant, transscleral cyclophotocoagulation

1 | INTRODUCTION

Glaucoma is a disorder of all species due to a rise of intraocular pressure (IOP) beyond which is compatible with ganglion cell and axon function, often resulting in optic nerve degeneration and irreversible blindness. The overall prevalence of primary and secondary glaucoma in the dog is similar to humans, at an estimated 1%-2%.[1] Compared with dogs, glaucoma is uncommon in feline patients, with a reported incidence of less than 0.3%, but there remain questions on its true incidence, as glaucoma often goes unrecognized in cats and is most commonly secondary to other intraocular disease.[2,3]

Medical and surgical interventions for glaucoma are aimed at lowering intraocular pressure through reducing the production of aqueous humor, increasing or altering the drainage mechanism for aqueous humor, or a combination of both. In the past 60 years, surgical interventions have progressed in both human and veterinary ophthalmology, but advancements in human surgical ophthalmic care are not interchangeable due to anatomical differences along the entire aqueous outflow pathway. Pectinate ligament dysplasia, a major risk factor for the onset of primary angle-closure glaucoma (PACG) of dogs, is a rare condition of humans. After the trabecular meshwork, humans have a Schlemm's canal, whereas it is replaced by the angular aqueous plexus in most species. Nonetheless, most often due to the financial commitment to develop new devices, veterinary ophthalmologists continue to look to MD ophthalmologists for novel surgical therapies.

In veterinary patients, surgical procedures are aimed at maintaining vision for as long as possible. When blindness ensues and pain persists, comfort procedures such as enucleation, intrascleral prosthesis, or chemical ablation are pursued; thus, procedures such as iridencleisis, corneoscleral trephination, and cyclodialysis that have shown failure to maintain vision in veterinary patients are no longer performed clinically.[4,5] The present article is intended to provide a concise review of current glaucoma surgical therapies in small animals.

2 | CYCLODESTRUCTIVE PROCEDURES

Aqueous humor formation can be reduced through destruction of the ciliary body epithelium with the application of cryotherapy[6-10] or laser therapy.[11-13] Regardless of technique, the three and nine o'clock positions are avoided to prevent damage to the long posterior ciliary arteries and veins.[6,9,10] Cryotherapy with nitrous oxide or liquid nitrogen was the mainstay of cyclodestructive techniques before lasers became readily available in clinical veterinary ophthalmology in the late 1980s. Common postoperative side effects of cyclocryotherapy include severe postoperative inflammation and immediate IOP spikes, variable IOP control, and sometimes resulting phthisis bulbi.[7,10,14]

Laser-assisted cyclodestruction with neodymium:yttrium aluminum garnet (Nd:YAG; 1064-nm wavelength) and diode (810-nm wavelength) has been described in small animals and equine patients.[4,11-13,15-25] Histologically, both laser applications similarly affect the ciliary body, but diode laser won popularity due to lower cost and absorption by melanin pigment yielding more numerous applications beyond glaucoma therapy.[16,26,27] As a noninvasive procedure with very little learning curve, transscleral cyclophotocoagulation (TSCPC) is more commonly performed. Positioning the laser probe 3 to 4 mm behind the limbus allows delivery of surgeon-selected diode laser energy to the ciliary body until approximately 50% to 75% of treatment sites illicit an audible "pop" indicative of ciliary body tissue explosion.[1,20,28] The reported success rates for controlling IOP with TSCPC alone vary greatly from 92% at 6 months to 30% at 24 months.[21,22] Short- and long-term complications are consistent with immediate IOP spikes, cataract formation, keratitis, corneal ulceration, and retinal detachment being most common related to the nonselective destruction of adjacent tissue.[16,20-22]

The newest technological device for TSCPC utilizes a micropulse diode laser (MicroPulse® Cyclo G6; Iridex).[29] Using short waves of energy, adjacent tissues are presumably spared from collateral damage.[25,29] Preliminary findings were promising with a reported 50% success rate of controlling IOP for primary glaucoma by Sapienza et al,[30] and a 42% success rate for IOP control and 50% maintenance of vision at 1 year by Sebbag et al[25]; however with continued use of the technology on additional cases, Micropulse diode laser therapy does not appear to be more effective than TSCPC (John Sapienza, personal communication), and it has been shown to cause corneal hypoesthesia with resulting tear deficiencies and neurotrophic ulcerative keratitis in some patients.[31]

For over 15 years now, veterinary ophthalmologists have been utilizing an endoscopic means for accessing the ciliary body for diode ablation (endolaser cyclophotocoagulation, ECP). Sometimes combined with phacoemulsification or lensectomy for better access to the ciliary body and to avoid lens trauma, the endoscopic visualization requires less laser energy and allows more controlled delivery, thus avoiding damage to surrounding tissues. Although no peer reviewed study has been completed, success for IOP control and maintenance of vision at 1 year postoperatively has been quoted at 85% and 71.8%, respectively.[32-35] Equipment cost and the associated surgical fees for intraocular delivery limit some practitioners from expanding to this technology. Postoperative uveitis is significant, and controlling it with multiple anti-inflammatories both topically and systemically is imperative for the best possible outcome.[28] The maximum IOP-lowering effects of ECP are not immediate, and frequent IOP evaluations for 2-3 weeks postoperatively are recommended with topical glaucoma therapy and aqueocenteses as needed.[28]

3 | FILTERING PROCEDURES

The placement of gonioimplants allows aqueous humor to be diverted from the anterior chamber to a unique anatomical space such as the frontal sinus, subconjunctival, suprachoroidal, or intrascleral space.[36] First described in 1998 with frontal sinus shunting, this "valved" system consists of a silicone tube in the anterior chamber with a valved tip and anchoring bulb in the frontal sinus.[37,38] Due to surgical complexity of placement and complication rates, frontal sinus shunts are now less commonly performed.

The general design of currently manufactured implants consists of a silicone, polypropylene, or polyethylene plate that ranges from 85 to 350 mm^2 with a silicone tube extension.[36] The internal diameter of the tube is 0.3 mm and allows the flow of aqueous humor from the anterior chamber through the tubing to the plate by either valved (Ahmed and Krupin)[5,35,36,39,40] or nonvalved (Baerveldt and Molteno)[41,42] mechanisms. Valved shunts open when IOP rises over approximately 12 mm Hg with subsequent "bleb" formation for systemic reabsorption.[43,44]

Ahmed gonioimplants are the most commonly utilized filtering device in clinical veterinary ophthalmology today.[36,40,45,46] A retrospective of 9 cases of Ahmed placement with concurrent mitomycin C usage performed over 8 years by Westermeyer et al demonstrated variable control of IOP with a median control of IOP for 326 days and a median interval to vision loss at 518 days. At 1 year post-op, 89% had maintained vision.[40] A larger study by Saito of 104 eyes of 97 dogs undergoing Ahmed gonioimplant placement alone with modifications including a large fornix-based flap with minimal tacking and a scleral tunnel demonstrated an unprecedented, and unrepeatable by most ophthalmologist's experience, vision in 80 of 87 eyes at 1 year, 41 of 55 at 2 years, 17 of 33 at 3 years, 12 of 21 at 4 years, and 4 of 12 at 5 years postsurgery.[39] A modified Ahmed implant for shunting aqueous humor to the ocular surface in a dog was described by Garcia da Silva in 2017,[45] but continuation of the technique on additional cases did not prove to be as effective as the first case, with failure of subsequent cases between 2 and 6 months postoperatively (Enry Garcia da Silva, personal communication).

Tinsley et al in 1994, and Graham et al in 2017, described the use of Baerveldt devices in dogs. In human glaucoma patients, they have been associated with higher long-term success and lower adjunctive medication requirements postoperatively. In their studies, 66%-80% maintained vision at the time of the last follow-up, but the average time to failure was a brief 83 days and almost all required multiple surgical revisions or experienced complications.[41,47]

In an attempt to increase long-term success rates for controlling IOP and maintaining vision in veterinary patients with glaucoma, a cyclodestructive procedure combined with a filtering procedure has been described.[24,48] In 1999, the combination of cyclocryotherapy or TSCPC with gonioimplantation was described by Bentley et al[24] Seven of 19 eyes still experienced immediate severe postoperative pressure spikes, but at 1 year postoperatively, 58% maintained vision and 74% IOP control. The largest retrospective by Sapienza and van der Woerdt involved 51 eyes of dogs that underwent TSCPC and Ahmed gonioimplants.[48] Short-term success was 82%, but by 6 months, only 49% maintained vision, and at 12 months, 41%. Complications for both studies were identical to those described for each technique individually with formation of fibrin, corneal ulceration, cataracts, implant bleb fibrosis, and recurrence of glaucoma being most common. The most recent study compared Baerveldt devices with TSCPC and placement of a suture shunt in dogs by Graham in 2018. Mitomycin C was utilized in most cases at the scleral bed where the Baerveldt devices were implanted and included the use of an intraluminal stent and partial ligation of the tube to prevent hypotony. While IOP control without loss of vision was more likely following Baerveldt implantation (60.7% compared with 35.2%), the author points out the retrospective nature of the study with inconsistencies in surgical techniques and postoperative protocols making it difficult for direct comparison.[41]

Regardless of technique, fibrosis at the site of diverted outflow (most commonly the subconjunctival) is one of the main reasons for implant failure in both human and veterinary patients. It is speculated that because of a more reactive uvea to insult/surgery, higher production of fibrin, and higher protein concentrations in the aqueous of nonprimates, fibrosis more quickly develops in veterinary patients.[49] Antifibrotic compounds such as mitomycin-C (MMC) or 5-fluorouracil (5-FU) are the most commonly utilized drugs at the time of surgery, but fibrosis is inevitable, even in the hands of the most experienced surgeons.[1,36,38-41,45]. Revision of the "bleb" and removal of fibrosis with repeated use of antifibrotic agents is often performed weeks to months after the initial surgery. A recent study shows promise for pirfenidone and its efficacy in decreasing fibrosis following shunt surgery with minimal side effects.[50]

4 | MINIMALLY INVASIVE GLAUCOMA SURGERIES (MIGS)

The newest modifications to gonioimplants in controlling IOP in humans with glaucoma involve minimally invasive glaucoma surgeries (MIGS). Those that are trabecular-based devices, to improve trabecular outflow through Schlemm's canal, cannot be extrapolated to veterinary ophthalmology due to anatomical differences already mentioned.[51]

The Ex-PRESS Mini-Glaucoma Device, however, is a nonvalved stainless steel implant derived in the age of MIGS with use in veterinary ophthalmology. The implant is inserted into the anterior chamber under a scleral flap for an attempt at lessening postoperative bleb failure. Lutz and Sapienza described its use combined with ECP in 4 cases in 2009 with a 75% control of IOP and 50% maintenance of vision at 1 year post-op with hypotony in 1 case and recurrence of glaucoma in another. There have been no further studies or reports of its use.[52]

Microfistula implants made of a glutaraldehyde cross-linked porcine gelatin tube (XEN model 45; AqueSys) have been manufactured in an attempt to diminish an inflammatory reaction. They have shown biocompatibility in rabbits and dogs, but their use in a clinical setting on glaucomatous veterinary patients has not been completed.[53]

The most recent filtering device proposed for dogs, the SalVO/Brown Glaucoma Implant (MicroOptx), routed aqueous humor from the anterior chamber directly onto the ocular surface. As a MIGS device, it showed promise with safety studies in normal Yucatan pigs[54,55] but a multicenter study that involved 65 implants showed a high incidence of complications including device extrusion, intractable uveitis, and endophthalmitis.[56]

5 | SUMMARY

Despite numerous surgical approaches, glaucoma in small animals remains a frustrating disease to treat. Future aims for glaucoma therapy in veterinary medicine will need to focus on procedures that take into account specifically the unique anatomy of our patients and the severe inflammatory response to ocular surgery. Prospective studies with newer gonioimplant technology alone and combined with cyclodestructive procedures may prove to be beneficial for the long-term success of this blinding condition.

CONFLICT OF INTEREST

None.

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