Canine Glaucoma: Medical and Surgical Treatment Options*

The goals of glaucoma therapy are to preserve or regain vision by maintaining normal intraocular pressure (IOP) and to alleviate pain. The therapeutic plan depends on the patient’s visual status, the chronicity of the condition, and the underlying cause (primary or secondary). Congenital glaucoma is rare and cannot be treated well.

Antiglaucoma Medications

Medications for glaucoma either decrease aqueous humor production or increase aqueous humor outflow. There is no single optimal therapeutic protocol for all dogs with glaucoma, and many patients require multiple medications. Studies of antiglaucoma medications show that dogs with glaucoma demonstrate a greater decline in IOP than do dogs with a normal IOP. TABLE 1 gives an overview of antiglaucoma medications.

Medications to Decrease Aqueous Humor Production

β Blockers

Betaxolol is a selective β1 antagonist that decreases the production of aqueous humor via β-adrenergic blockade in the ciliary body. A large clinical trial in dogs demonstrated that predisposed eyes treated topically with 0.5% betaxolol twice daily as a prophylactic glaucoma therapy developed glaucoma much later than nontreated eyes. Timolol maleate is a nonselective β antagonist. Topical administration of timolol causes mild miosis in dogs and may increase aqueous humor outflow in addition to inhibiting production. Both β1-selective and nonselective β antagonists may have undesirable cardiac effects, including bradycardia, syncope, or reduced myocardial contractility. Additionally, blockade of β2 receptors by nonselective β blockers could produce adverse respiratory effects, especially in patients with asthma, so timolol should not be used in dogs with cardiac or pulmonary disease.

Carbonic Anhydrase Inhibitors

Systemic and topical carbonic anhydrase inhibitors (CAIs) are available. Inhibition of carbonic anhydrase decreases aqueous humor production by reducing the syn-
thesis of bicarbonate in the ciliary body.\textsuperscript{1,2}

The oral CAIs acetazolamide and methazolamide can have systemic adverse effects. Acetazolamide is no longer recommended due to the high incidence of such effects. Adverse effects associated with the use of methazolamide include gastrointestinal upset, metabolic acidosis, and hypokalemia.\textsuperscript{5}

Topical CAIs reach adequate ciliary body concentrations and have a lower risk of systemic adverse effects. Brinzolamide significantly reduces IOP in dogs with glaucoma.\textsuperscript{1} Dorzolamide has been shown to reduce IOP as effectively as methazolamide with many fewer systemic effects. No additional decline in IOP is obtained from the combination of an oral CAI with a topical CAI; therefore, we recommend the use of a topical CAI for long-term management.\textsuperscript{6,7} The most common adverse effect of topical dorzolamide is transient blepharospasm after instillation.\textsuperscript{7,8}

A solution of 2\% dorzolamide and 0.5\% timolol maleate is available. This combination therapy is as efficacious in reducing IOP as concurrent use of each drug,\textsuperscript{9} but the commercially available combination improves client compliance because it requires only twice-daily administration.\textsuperscript{8,9}

\begin{table}[h]
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\caption{Antiglaucoma Medications\textsuperscript{1,8,a,b}}
\begin{tabular}{|c|c|c|c|}
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\textbf{Drug} & \textbf{Available Preparations} & \textbf{Recommended Dose or Timing} & \textbf{Contraindications} \\
\hline
\textbf{β Blockers} & & & \\
Betaxolol & 0.25\% and 0.5\% solutions & q12h & Keratoconjunctivitis sicca, cardiac or respiratory disease \\
Timolol maleate & 0.25\% and 0.5\% solutions & & \\
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\textbf{Carbonic anhydrase inhibitors} & & & \\
Methazolamide & 25- and 50-mg tablets & 2.5–5 mg/kg q8–12h PO & Hypokalemia, metabolic acidosis \\
Brinzolamide & 1\% solution & q8h & None, but may cause irritation shortly after instillation \\
Dorzolamide & 2\% solution & & None, but may cause irritation shortly after instillation \\
Dorzolamide–timolol maleate & 2\% dorzolamide and 0.5\% timolol maleate & q12h & Keratoconjunctivitis sicca, cardiac or respiratory disease \\
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\textbf{Cholinergics} & & & \\
Pilocarpine & 1\% solution & q8–12h & Anterior lens luxation, uveitis \\
Demecarium bromide\textsuperscript{c} & 0.125\% and 0.25\% solutions & q12–24h & \\
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\textbf{Prostaglandin analogues} & & & \\
Latanoprost & 0.005\% solution & q12–24h & Severe uveitis, anterior lens luxation \\
Travoprost & 0.004\% solution & & \\
Bimatoprost & 0.03\% solution & & \\
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\textbf{Hyposmotic agents} & & & \\
Mannitol & 20\% solution & 1–1.5 g/kg IV slowly over 20 min & Cardiac or renal disease, dehydration \\
Glycerin & 50\% and 75\% solutions & 1–2 g/kg PO & Cardiac or renal disease, diabetes mellitus, dehydration \\
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\textsuperscript{b}Medications are topical ophthalmic preparations unless otherwise noted.

\textsuperscript{c}Must be compounded.
Other Medications

α, Agonists and epinephrine have historically been used to treat glaucoma, but with recent advances in glaucoma therapy, other drugs with increased efficacy and fewer potential adverse effects (β blockers, CAIs) may be more appropriate.8,10,11

Medications to Increase Aqueous Humor Outflow

Cholinergic Agents

Parasympathomimetics are used in the treatment of canine glaucoma except when intraocular inflammation is present. Parasympathomimetics are used in long-term management of canine glaucoma and are often combined with CAIs and/or β blockers to improve IOP control.1 They induce contraction of the ciliary body musculature and severe miosis, which subsequently opens the drainage angle, facilitating aqueous humor outflow. Parasympathomimetics are contraindicated in dogs with anterior lens luxation and anterior uveitis.

Pilocarpine is a direct-acting parasympathomimetic that simulates the action of acetylcholine on the iris and ciliary body.2 Because of the nonphysiologic pH of the solution, topical administration causes irritation in most dogs; therefore, this drug is not generally recommended as a first-line therapy.1,5

Demecarium bromide is an indirect-acting parasympathomimetic that increases the duration of the acetylcholine normally produced in the ciliary body. The main advantage of demecarium bromide is its long duration of action. Demecarium bromide 0.25% has been shown to significantly delay the onset of primary glaucoma in predisposed eyes when used in combination with a topical steroid.3 Demecarium bromide 0.125% and 0.25% are available from compounding pharmacies. Topical demecarium bromide can reach systemic concentrations high enough to result in toxicosis. Although this adverse effect is uncommon, the drug should be used with caution in small dogs.12 Signs of toxicosis include diarrhea, salivation, and vomiting.2

Prostaglandin Analogues

Prostaglandin analogues are the newest topical glaucoma drugs used in dogs. They are thought to lower IOP primarily by increasing uveoscleral outflow of aqueous humor via their action on iris and ciliary body musculature; however, research shows an effect on the conventional outflow pathway as well.13 These drugs may also cause a reduction in aqueous humor production.14 Prostaglandin analogues should be avoided in cases of glaucoma secondary to anterior lens luxation or uveitis. Latanoprost is a selective prostaglandin Fα receptor agonist that results in a dramatic decrease in IOP within 20 minutes.15 Travoprost and bimatoprost are newer prostaglandin analogues shown to be efficacious in dogs.1

Hyperosmotic Agents

Hyperosmotic agents reduce the production of aqueous humor by reducing plasma flow through the ciliary body, thereby dehydrating the vitreous.5 The main indication for the use of hyperosmotic agents in canine glaucoma is emergency management of increased IOP. For maximum efficacy, water should be withheld for 4 hours after administration.

Mannitol is an osmotic diuretic that has been shown to significantly reduce IOP within 15 minutes of administration and can remain effective for 6 to 10 hours.16 Mannitol can be used safely in most dogs but should not be used in dogs with cardiac or renal disease or in dehydrated patients.

Oral glycerin causes a significant decrease in IOP within 30 minutes of administration and has a duration of effect of 10 hours.16 Glycerin should not be used in dogs with diabetes mellitus. The most common side effect of oral administration is gastrointestinal upset.

In an emergency situation, we recommend starting with a topical prostaglandin analogue. The IOP should be rechecked after 20 to 30 minutes. If it is still elevated, an osmotic diuretic may be indicated. After application of a topical prostaglandin analogue, a topical CAI can be administered to gain further control of the IOP. If not contraindicated, a topical β blocker can also be administered.

Surgery for Glaucoma

When medical therapy can no longer control the IOP, surgery may be indicated. The time for which medical therapy is effective depends on the individual patient. If the IOP becomes uncontrollable or the dog is uncomfortable, early referral to a veterinary ophthalmologist for surgical management is ideal. Some surgical procedures that can alleviate pain associated with end-stage glaucoma in nonvisual eyes

Many patients with glaucoma require multiple medications.
can be performed by a general practitioner. As with medical therapy, surgical procedures to address glaucoma either reduce aqueous humor production or improve aqueous humor outflow. The procedure chosen depends on the dog’s visual status and the desired cosmetic outcome. Medical therapy is usually still necessary after procedures that preserve vision.

**Surgery to Decrease Aqueous Humor Production**

Cyclodestruction, or destruction of the ciliary body, decreases the production of aqueous humor and can be performed using cryotherapy, transscleral lasers, or endoscopic cyclophotocoagulation.

Cyclocryotherapy uses either liquid nitrogen or nitrous oxide applied to the sclera by a probe to cause cryonecrosis of the ciliary body. Cryotherapy can cause severe uveitis, cataracts, and retinal detachment and is therefore not generally recommended in visual eyes.\(^1\)

Transscleral cyclophotocoagulation (TSCP) uses a diode or Nd:YAG laser to irradiate the ciliary body. Studies have shown this procedure to be effective in controlling IOP.\(^{17,18}\) The most common complications of TSCP are recurrence of glaucoma requiring a second procedure, secondary cataract formation, and ulcerative keratitis.\(^{19}\) This procedure may be combined with implantation of an anterior chamber shunt (gonioimplant) for better control of postoperative IOP spikes. Two studies have shown the combination procedure to be successful, with up to 58% of dogs retaining vision after 1 year.\(^{18,20}\)

One of the main disadvantages of the non-invasive cyclodestructive techniques is the inability to see the extent of destruction of the ciliary body. Endoscopic cyclophotocoagulation (ECPC; endolaser) uses a diode endoscopic laser to deliver energy to the ciliary body. Most patients require phacoemulsification and intraocular lens implantation before the procedure to prevent cataract formation. Other reported complications include uncontrolled IOP, corneal ulceration, retinal detachment, and hyphema secondary to postoperative hypotony. This procedure offers a high success rate of IOP control and vision preservation and may allow a decrease in antiglaucoma medications. In a study of 106 dogs with primary and secondary glaucoma, 93% of dogs treated with ECPC had controlled IOPs at 1 year and 77% retained vision at 1 year.\(^4\)

**Surgery to Increase Aqueous Humor Outflow**

Currently, gonioimplants and the Cullen frontal sinus shunt are the most commonly used shunts in veterinary ophthalmology. Gonioimplants consist of an implant and tubing that allows aqueous humor to drain from the anterior chamber into the subconjunctival space. Gonioimplants can be combined with surgical techniques to decrease aqueous humor production but usually do not suffice for sole long-term management. The Cullen frontal sinus shunt is a valved tube that is anchored into the frontal sinus and directed into the anterior chamber of the eye.\(^{21,22}\) Complications of shunting procedures include occlusion of the tube with fibrin, fibrosis around the implant, extrusion of the implant, and postoperative hypotony.\(^{1,22,23}\)

**Salvage Procedures**

Chronic end-stage glaucoma may be painful, and buphthalmic globes are predisposed to exposure keratitis. Surgical options for chronically glaucomatous globes include enucleation, evisceration with intrascleral prosthesis, and chemical ablation.

**Enucleation**

Enucleation is relatively inexpensive and has few complications. An orbital prosthesis may be placed to improve the cosmetic appearance. The main disadvantage of enucleation is the postoperative appearance of the patient. The benefits include the potential for histopathologic examination of the globe and immediate pain control.\(^1\)

**Intrascleral Prosthesis**

Evisceration and intraocular placement of a silicone ball has a 95% success rate and, often, very good cosmetic results. Postoperative complications are minimal but may include corneal ulcers and persistent corneal edema.\(^1,23\)

**Chemical Ablation**

Pharmacologic destruction of the ciliary body is accomplished by injecting gentamicin and dexamethasone into the vitreous cavity. Complications include inadequate control of IOP,\(^a\)

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hyphema, uveitis, retinal detachment, cataract development, and phthisis bulbi.23

**Conclusion**

Canine glaucoma is difficult to manage, but there are many therapeutic options. Owner expectations, visual status, and cause of the disease help dictate the appropriate treatment course.

**References**

1. The goal of therapy for canine glaucoma is to
   a. preserve or regain vision in the eye.
   b. maintain normal IOP.
   c. alleviate pain.
   d. all of the above

2. The treatment of glaucoma should aim to increase; increase the production and/or decrease the outflow of aqueous humor.
   a. increase; increase
   b. decrease; increase
   c. decrease; decrease
   d. increase; decrease

3. Which statement regarding topical β blockers is true?
   a. Betaxolol is a nonselective β antagonist.
   b. Timolol maleate is a selective β₁ antagonist.
   c. β Blockers decrease the production of aqueous humor via β-adrenergic blockade in the cornea.
   d. β Blockers are contraindicated in patients with cardiac or respiratory disease.

4. Which statement regarding CAIs is true?
   a. Brinzolamide and dorzolamide are topical medications that reduce systemic side effects while achieving adequate ocular concentrations.
   b. CAIs increase the production of aqueous humor by reducing synthesis of bicarbonate in the ciliary body.
   c. Common side effects of oral CAIs include gastrointestinal upset, metabolic alkalosis, and hyperkalemia.
   d. Of the oral CAIs, acetazolamide is preferred to methazolamide because it is associated with fewer adverse effects.

5. Which statement regarding parasympathomimetics is true?
   a. Parasympathomimetics are contraindicated for use in patients with uveitis or anterior lens luxation.
   b. Parasympathomimetics lower IOP by inducing mydriasis, therefore opening the iridocorneal angle.
   c. Pilocarpine is generally well tolerated by most dogs.
   d. The main advantage of demecarium bromide is its short duration of action.

6. Which statement regarding prostaglandin analogues is true?
   a. They are thought to increase uveoscleral outflow of aqueous humor.
   b. They may decrease IOP by reducing the production of aqueous humor.
   c. They are contraindicated for use in patients with uveitis or anterior lens luxation.
   d. all of the above

7. Which statement regarding hyperosmotic agents is true?
   a. Hyperosmotic agents reduce the formation of aqueous humor by increasing plasma flow through the ciliary body.
   b. Hyperosmotic agents are indicated for long-term control of glaucoma.
   c. Mannitol decreases IOP within 15 minutes of administration, but its effect only persists for approximately 1 hour.
   d. Oral glycerin is contraindicated in diabetic patients.

8. Surgical treatment of canine glaucoma
   a. should not be performed in visual eyes.
   b. can alleviate pain associated with end-stage glaucoma in blind eyes.
   c. can decrease the production or increase the outflow of aqueous humor, depending on the technique chosen.
   d. b and c

9. Which statement regarding cyclodestructive techniques is true?
   a. Destruction of the ciliary body can be accomplished using cryotherapy, transscleral lasers, or endoscopic cyclophotocoagulation.
   b. Cyclocryotherapy has few complications and is thus considered a safe procedure for all patients with glaucoma.
   c. Transscleral cyclophotocoagulation may induce cataract formation.
   d. a and c

10. Which statement regarding salvage surgical procedures for glaucoma is true?
    a. Enucleation is relatively inexpensive and has few complications.
    b. Evisceration and placement of an intrascleral prosthesis improves the cosmetic appearance.
    c. Complications of chemical ablation of the ciliary body include inadequate control of IOP, hyphema, uveitis, retinal detachment, cataract formation, and phthisis bulbi.
    d. all of the above