



Time to failure of prophylactic topical timolol therapy in dogs with primary angle closure glaucoma



Breanna Fox and Jessica Meekins

Kansas State University College of Veterinary Medicine
Department of Clinical Sciences

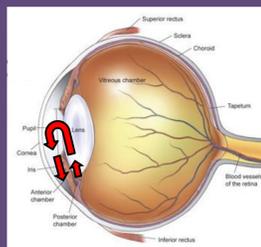
Introduction

Glaucoma is widely recognized as a disease resulting in an increase in intraocular pressure (IOP), causing damage to the optic nerve (Foster et al., 2002). There are primary and secondary forms of glaucoma. Primary glaucoma is typically associated with certain breeds, is bilateral, and has a genetic basis (Paul E. Miller & Bentley, 2015), while secondary glaucoma is often associated with other ocular diseases that alter the normal flow of fluid in the eye (Pumphrey, 2015). Primary glaucoma in dogs can be either closed angle (PACG) or open angle (POAG), with closed angle glaucoma occurring much more commonly (P. E. Miller et al., 2000).



Canine eye with acute glaucoma
Courtesy of Dr. Jessica Meekins

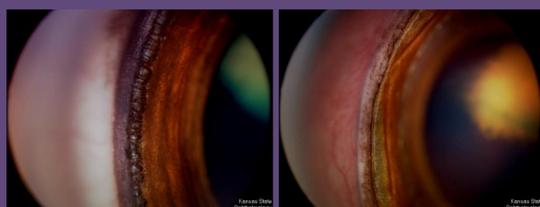
This form of glaucoma often seems to occur spontaneously and is thought to be due to heritable traits affecting the drainage of aqueous humor, the fluid located in the anterior and posterior chambers of the eye (Pizzirani, 2015). This fluid is responsible for maintaining appropriate pressure within the eye and providing nutrition to avascular ocular structures. The aqueous humor is produced by the ciliary body and is first released into the posterior chamber. It then flows through the pupil and into the anterior chamber where, under normal conditions, the fluid then drains out of the eye via the iridocorneal angle (ICA). In dogs with PACG, the opening of this drainage angle is malformed, causing blockage of fluid outflow and inadequate drainage. As fluid outflow is impaired, pressure builds within the eye, resulting in damage to ocular structures including the optic nerve.



Flow of aqueous humor in the canine eye
Courtesy of Dr. Jessica Meekins

In dogs affected by PACG, the angle opening will appear narrowed or closed (i.e., pectinate ligament dysplasia, or goniodysgenesis) upon direct examination of the ICA (called gonioscopy). This form of glaucoma manifests as a rapid and significant unilateral increase in IOP. Due to the heritable and bilateral nature of the pectinate ligament dysplasia resulting in abnormal draining of aqueous humor, the fellow eye is at risk for and will ultimately develop PACG (P. E. Miller et al., 2000). Miller et al. found in a clinical trial that prophylactic anti-glaucoma therapy in PACG can prolong the health of the fellow eye.

In that study, dogs in the control group receiving no treatment developed PACG in the remaining eye at a median of eight months from initial diagnosis, while dogs treated prophylactically were able to maintain a healthy IOP for a median of 31 months (P. E. Miller et al., 2000).



Normal (left) canine ICA opening as viewed by gonioscopy vs. goniodysgenesis (right) in a canine eye
Courtesy of Dr. Jessica Meekins

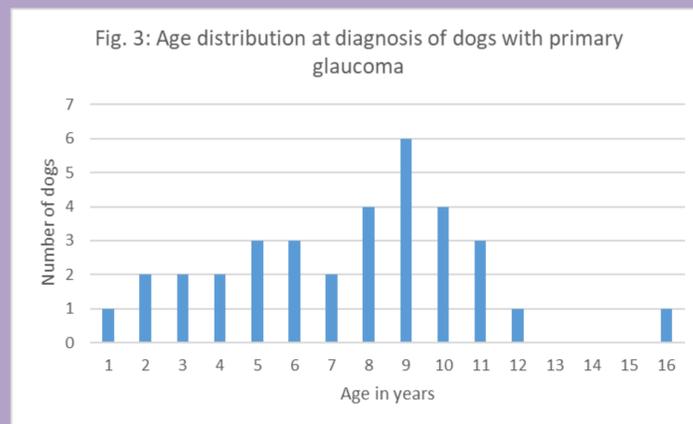
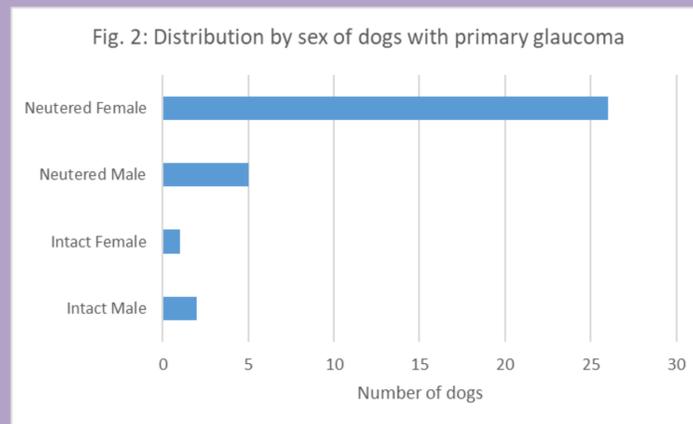
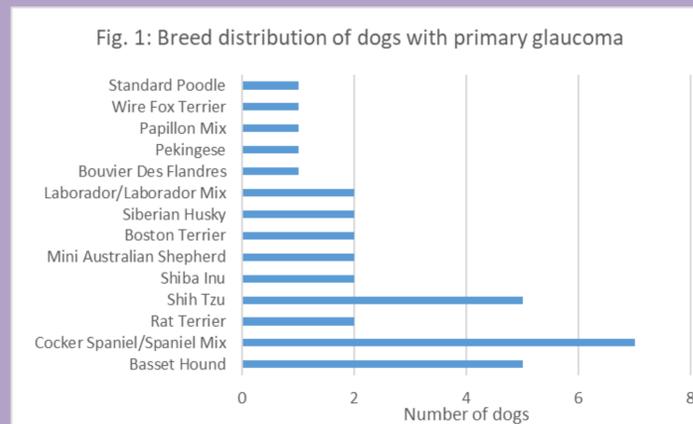
Miller et al. looked at the effects of betaxolol, a beta-1-adrenergic antagonist, as an anti-glaucoma prophylactic treatment. Other investigators have evaluated the effects of other treatments such as carbonic anhydrase inhibitors (Stavinohova et al., 2015). Timolol, the drug investigated in our study, is a nonselective beta adrenergic antagonist that effectively lowers IOP in normal dogs and dogs with PACG (P. E. Miller et al., 2000). It is unknown, however, how long timolol can be expected to prolong the normotensive condition of the fellow eye in dogs diagnosed with PACG. It is also of interest to investigate any benefit of regular IOP rechecks in delaying onset of PACG in dogs that have not yet developed glaucoma in the fellow eye, as this is currently standard practice.

Materials and Methods

A retrospective search of patients presented to Kansas State University's Veterinary Health Center (KSU VHC) over an 11-year period (2009 – 2020) was performed. Canine patients diagnosed with PACG (based on histopathology or clinical signs and gonioscopy of the fellow [pre-glaucoma] eye) and treated prophylactically with 0.5% timolol maleate ophthalmic solution were included. 34 client-owned dogs met these criteria. Dogs diagnosed with secondary glaucoma, with bilateral signs of glaucoma, those prescribed multiple prophylactic anti-glaucoma medications, and those not diagnosed with primary glaucoma by a veterinary ophthalmologist were excluded. Categories of data collected for each patient included age, breed, reproductive status, eye treated prophylactically, date of treatment initiation, date of treatment failure, frequency of treatment, and number of rechecks during treatment. All dogs included in this study were administered treatment twice a day with a single drop of timolol in the eye requiring prophylaxis. Failure of treatment was considered to occur when PACG was diagnosed in the eye receiving prophylaxis. A diagnosis of PACG was made based on a documented increase in IOP using tonometry and clinical signs of acute glaucoma as determined by a veterinarian. Follow-up for cases not returning to KSU VHC for all rechecks will be achieved by contacting primary/referring veterinarians to confirm dates of treatment failure and number of rechecks prior to failure.

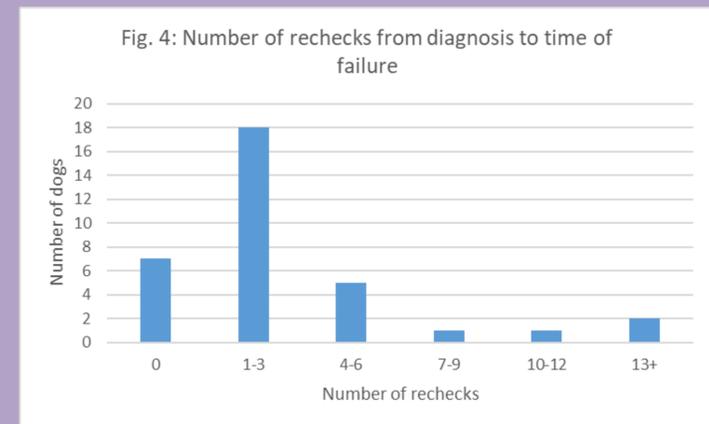
Results

34 client-owned dogs diagnosed with PACG were identified from KSU VHC patient records. Represented breeds are shown in Figure 1, while Figures 2 and 3 respectively show the ratio of males to females and the reported age at onset of glaucoma for each patient.



Spayed females were overrepresented in our study population, and several breeds (e.g., Cocker Spaniels, Basset Hounds, Shih Tzus) commonly recognized as affected by PACG were identified. The mean age at diagnosis of the dogs in this study was 7.8 years old. Preliminary results revealed a mean of 7.2 months until failure of timolol therapy for 23 cases, with time to failure ranging from 0.5-37.6 months. Six of these cases are expected to be deceased based on recorded date of birth in KSU VHC medical records, leaving 17 cases with definitively confirmed treatment failure based on our records.

Follow-up confirmation with primary/referring veterinarians is pending to determine health status and time to treatment failure on all cases with incomplete follow-up at KSU VHC. We expect to modify the mean time to treatment failure based on additional case information. Eleven cases have not yet experienced a spike in IOP based on KSU VHC records. The mean time since diagnosis of PACG in those cases is 30.1 months, with a range of 8.2-65.3 months. Of the 17 patients that have experienced a KSU VHC confirmed spike in IOP, the mean number of rechecks prior to treatment failure was 3.7, ranging from 0-37 (Figure 4).



Conclusions

Preliminary results indicate that timolol therapy is effective at delaying the onset of glaucoma when used prophylactically in the healthy pre-glaucoma eye of dogs with PACG. The goal of this study is to provide veterinarians with information about how long timolol can be expected to delay the onset of PACG, as it is a readily available, affordable medication in veterinary practice. The mean time since diagnosis of 30.1 months in a subset of our cases that have yet to fail treatment indicates that timolol, a non-selective beta antagonist, is as effective as betaxolol, a selective beta antagonist proven to help maintain a normal IOP in the healthy eye of dogs with PACG.

Acknowledgements

- Boehringer Ingelheim Veterinary Scholars Program
- KSU Veterinary Research Scholars Program

References

1. Foster PJ et al. *The British journal of ophthalmology*. 86(2):238-242 (2002).
2. Miller, P. E. et al. *Journal of the American Animal Hospital Association*. 36(5), 431-438 (2000).
3. Miller, Paul E., & Bentley, E. *Veterinary Clinics of North America - Small Animal Practice*. 45(6), 1183-1212 (2015).
4. Pizzirani, S. *Veterinary Clinics of North America - Small Animal Practice*. 45(6), 1127-1157 (2015).
5. Pumphrey, S. *Veterinary Clinics of North America - Small Animal Practice*. 45(6), 1335-1364 (2015).
6. Stavinohova, R. et al. *Journal of Small Animal Practice*. 56(11), 662-666 (2015).