Effect of topical diclofenac 0.1% ophthalmic solution on tear production in normal research beagles when administered SID, BID, TID & QID for 5 days

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Introduction

- Topical non-steroidal anti-inflammatory drugs (NSAIDS), such as diclofenac 0.1% ophthalmic solution, are commonly used for ocular inflammatory diseases in veterinary ophthalmology. No studies have examined the effect of this drug on tear production in dogs.
- The purpose of this study was to determine the effect of topical diclofenac on tear production in normal dogs when administered SID, BID, TID, and QID for a 5-day period. The hypothesis is that high frequency of topical diclofenac will have no effect on tear production and that it is safe to use this medication up to four times a day in dogs.

Fig 1.
Schirmer's tear test-I (STT-I) being performed. Tear production was measured using a standardized STT tear strip placed in the ventrolateral conjunctival fornix for one minute and the eyelids were lightly held closed throughout the test

Method and materials

- A prospective study with eight normal research beagles. The study consisted of four periods of 5-day studies (Day-1 to Day-5) where dogs received one drop of topical diclofenac sodium 0.1% ophthalmic solution (Alcon, Fort Worth, TX) to OD (test-eye) and one drop of eye wash to OS (control-eye) using SID, BID, TID, and QID frequencies with a 16-day washout period between each study.
- A complete ophthalmic examination was performed including Schirmer's tear test-I (STT-I) and fluorescein stain the day before each study started (Day-0) and on the last day of each study (Day-5).
- Mean and standard deviation were measured for all STT-I values, and a linear mixed effect model was used for statistical analysis between eyes (OD-test (diclofenac) versus OS-control (eye wash)), baseline (Day-0 versus Day-5), and treatment frequencies (Study 1=SID, Study 2=BID, Study 3=TID, Study 3=QID).

Results

- All dogs' STT-I values were above 15 mm/min for all treatment frequencies (SID, BID, TID, QID). OD-test eye STT-I values were slightly lower than OS-control eyes for Day-0, Day-5, and overall.
- For both eyes, Day-0 measurements were higher than Day-5 measurements except with treatment frequency of SID (Figure 2). Considering STT-I measurement on Day-5 as the variable of interest, there was not a significant interaction between treatment (OD-test (diclofenac), OS-control (eyewash)) and treatment frequency (SID, BID, TID, QID) which indicates changes in average STT-I values on Day-5 between eyes do not significantly differ among treatment frequency.
- There was a significant interaction between baseline measure and treatment (p=0.0399), indicating that changes in average Day-5 STT-I values between eyes differ according to baseline measure. For all treatment frequencies, lower Day 0 STT-I for the treatment eye has lower Day 5 STT-I while higher Day 0 STT-I for the treatment eye has higher Day 5 STT-I (Figure 3).

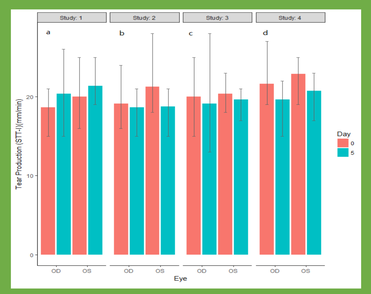

Figure 2. Average (±standard deviation) STT-I for 8 normal research beagle dogs and treatment applied a) Study 1 = SID; b) Study 2 = BID; c) Study 3 = TID; d) Study 4 = QID; OD-test eye given diclofenac 0.1% ophthalmic solution, OS-control eye given eye wash.

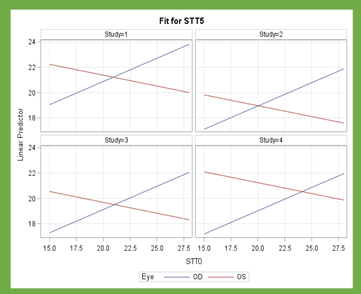

Figure 3: All treatment frequencies showed that a lower Day 0 STT-I for the treatment eye has lower Day 5 STT-I while higher Day 0 STT-I for the treatment eye has higher Day 5 STT-I

- After adjustment for the Day-0 measurements (baseline covariate), the mean STT-I taken on Day-5 for OS-control eye (eye wash) is greater than OD-test eye (diclofenac) except when treatment was given two times per day (BID) (Figure 4) but these differences were not significant (all p>0.05).

- No eyes (OD or OS) had positive fluorescein stain at Day-0 or Day-5.

Conclusion

- Tear production in eyes administered topical diclofenac for 5 days at varying intervals did not significantly differ from those administered eyewash.
- A significant difference was found between the baseline STT-I and 5-day values for eyes treated with diclofenac or eyewash. This indicates that changes in average Day-5 STT-I values between eyes differ according to baseline measure, not diclofenac administration.
- All STT-I values were above 15mm/min in all eyes (both OD-test (diclofenac), OS-control (eyewash)), and diclofenac did not cause positive fluorescein stain in normal dogs after 5 days of treatment. Clinically, this means that it seems to be safe to use topical diclofenac multiple times a day without causing tear production below 15mm/min or corneal ulcerations.

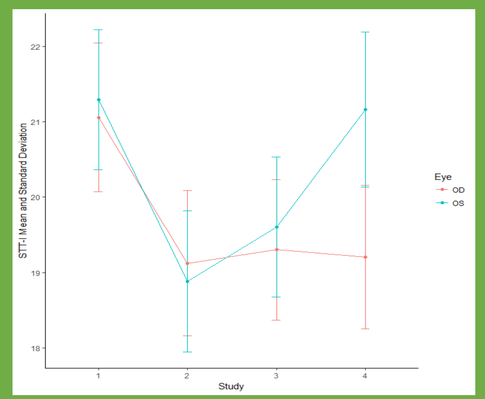

Figure 4. Plot of STT-I means (bars represent standard deviation) adjusted for baseline STT-I covariate by treatment frequency (i.e., Study) for each eye; OD-test eye given diclofenac 0.1% ophthalmic solution, OS-control eye given eye wash.

References

Giuliano (1) EA. Diseases and surgery of the canine lacrimal secretory system. In: Veterinary Ophthalmology, 5th edn. (eds Gelatt KN, Gilger BC, Kern TJ) Wiley-Blackwell, Hoboken, NJ, 2013; 912–944.

Sanchez RF, Innocent G, Mould J et al. Canine keratoconjunctivitis sicca: disease trends in a review of 229 cases. Journal of Small Animal Practice 2007; 48: 211–217.

Williams DL. Immunopathogenesis of keratoconjunctivitis sicca in the dog. Veterinary Clinics of North America Small Animal Practice 2008; 38: 251–268.

Giuliano (2) EA. Nonsteroidal anti-inflammatory drugs in veterinary ophthalmology. Veterinary Clinics of North America Small Animal Practice 2004; 34: 707–723.