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Update on Ophthalmic Medications

Presented 10/07/09 by

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The use and availability of ophthalmic medications is always changing, with old standards having new uses and new medications replacing our old favorites. The purpose of this lecture is to discuss some of my favorite medications, update you on their use, as well as discuss new medications that are helping treat our most difficult cases. Finally, I would like to introduce you to a new medication that has the potential to decrease the progression of diabetic cataracts.

1. Terramycin: Oxytetracycline PLUS polymyxin B

- ▶ Polymyxin B: A polypeptide antibiotic with a narrow gram-negative spectrum
- ▶ Oxytetracycline: From the tetracycline family, a bacteriostatic, broad spectrum antibiotic. Inhibits bacterial protein synthesis by blocking transfer RNA from binding to the ribosomal complex. Overall, oxytetracycline is a weak topical antibiotic for corneal disease in dogs and cats
- ▶ Benefits: Tetracyclines have immuno-modulating factors and alter corneal proteins/enzymes that are involved in corneal wound healing.
 - a. Inhibit matrix metalloproteinases 2 and 9, as well as several collagenases including neutrophil collagenase, epithelial gelatinase, and α 1-antitrypsin.
 - b. Stimulate transforming growth factor-beta and SLUG transcription factor to increase corneal epithelial cell migration.
- ▶ What this means:
 - a. STOP corneal melting
 - b. PROMOTE corneal wound healing
- ▶ When to use:
 - a. MELTING or severely infected corneal ulcers
 - b. INDOLENT corneal ulcers***
Recent abstract by Chandler et al (ACVO proceedings 2008) demonstrated faster healing times with terramycin vs. other topical antibiotics.

2. Tacrolimus: also known as FK-506 or Fujimycin

▶ An immunosuppressive drug similar to cyclosporine. It acts through an alternate pathway than cyclosporine to achieve a similar result: reducing T cell activation through inhibiting interleukin-2 activity.

▶ Benefits:

- a. Reduces T cell activation promoting surface immunosuppression.
- b. Direct lacrostimulant effects (as demonstrated by the ability to increase aqueous tear production in normal eyes).
- c. Increases conjunctival goblet cell density and mucin secretion
- d. Inhibits fibroblast proliferation

▶ What this means:

- a. Increases aqueous tear production in cases of dry eye, including those nonresponsive to topical cyclosporine (Berdoulay et al. 2005, Vet Ophthalmology demonstrated 51% of cases improved with topical tacrolimus that were previously nonresponsive to cyclosporine).
- b. Improves tear film quality by increasing tear film break up time. Less tear film evaporation leading to better corneal coverage and overall health.
- c. Decreases scar tissue formation following corneal ulcers, corneal surgery, etc.

▶ When to use:

- a. DRY EYE nonresponsive to cyclosporine
- b. Immune-mediated corneal and conjunctival disease
 - a. PANNUS
 - b. NGE
- c. Following healing of severe corneal ulcers to reduce scarring

3. Zymar (gatifloxacin) and Vigamox (moxifloxacin):

▶ Fourth generation (Zymar) and third generation (Vigamox) fluoroquinolone topical antibiotics. Inhibit DNA gyrase and topoisomerase IV to block cell division.

▶ Benefits:

- a. Gram positive AND Gram negative spectrum.
- b. Penetrate through an intact corneal epithelium.
- c. Little to no resistance***
 - a. **Currently, although it is our responsibility to not use these drugs indiscriminately or resistance will develop.

▶ What this means:

- a. Effective against the most common corneal invaders in dogs (*Staph* and *Strep*)
- b. Effective for stromal abscesses
- c. Some use for endophthalmitis as levels within the aqueous humor are high enough for MIC for many bacteria
- d. Unlike ciprofloxacin, it is well tolerated and does not “sting” the eye.

- ▶ When to use:
 - a. SEVERELY INFECTED corneal ulcers
 - b. MELTING corneal ulcers
 - c. Stromal abscesses
 - d. ***NEVER NEVER NEVER use on a simple, superficial corneal ulcer

4. Famvir: Famciclovir

▶ Pro-drug of penciclovir, which is a guanine analog. As a purine analog, it inserts itself in place of guanine and inhibits herpes viral replication.

- ▶ Benefits:
 - a. Oral medication (can be compounded as a liquid)
 - b. Increased plasma levels promoting more complete systemic herpetic control
 - c. Better efficacy against FHV in vitro compared to other available anti-virals
 - d. Well tolerated with very few systemic side-effects (infrequent GI)

- ▶ What this means:
 - a. Alternative to topical idoxuridine or trifluridine therapy
 - b. BETTER response to therapy, clearing of herpetic disease sooner.

- ▶ When to use:
 - a. Chronic, recurrent herpetic keratoconjunctivitis
 - b. Herpetic keratoconjunctivitis not responsive to topical anti-virals
 - c. Severe herpetic cases with ocular and dermatologic signs

5. Kinostat: Aldose reductase inhibitor

▶ Seventy-five percent of diabetic dogs will develop cataracts within one year of being diagnosed with diabetes. Diabetic cataracts occur due to a shift in the metabolic pathways within the lens, specifically a shift from glycolysis to the sorbitol shunt. This promotes increased levels of sorbitol within the lens, leading to an osmotic gradient, lens fiber swelling, and cataract formation. The enzyme, aldose reductase, is responsible for the formation of sorbitol. Inhibiting this enzyme may be an effective means to stop diabetic cataracts from forming.

- ▶ Benefits:
 - a. Topical medication used TID in early diabetic cases
 - b. 72% of diabetic dogs treated did NOT develop cataracts within 1 year.

- ▶ What this means:
 - a. Diabetic dogs may retain vision LONGER
 - b. Diabetic dogs may NOT need cataract surgery

- ▶ When to use???

 - a. Unfortunately we can't use this medication yet, as it is not commercially available.