Recent treatment developments for the animal eye

Cutting Edge Veterinary Ophthalmology

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Topics

- New medications
  - Diabetic cataracts
  - Nonresponse keratoconjunctivitis sicca

- Surgeries
  - Prolapsed third eyelid gland
  - Everted third eyelid cartilage
Diabetic cataracts
Diabetic cataracts

- VERY prevalent (Beam et al, 1999)
  - 50% within 6 months of diagnosis
  - 80% within 15 months of diagnosis

- Develop quickly
  - Intumescence
  - Spontaneous lens capsule ruptures
  - Poor compensation
How does diabetes mellitus cause cataracts?

- Anaerobic metabolism of glucose saturated
  - Hexokinase pathway
- Aldose reductase pathway
Diabetic cataracts

- Aldose reductase
  - Higher levels in the canine lens
  - Glucose -> Sorbitol
  - Osmotic gradient created
    - “Osmotic stress”
Diabetic cataracts
Diabetic cataracts

- So why are we talking about this?
  - 2-Methyl Sorbinil
Diabetic cataracts

- So why are we talking about this?
  - Kinostat
Aldose reductase inhibitor

- Prevents sorbitol accumulation
- Requires constant inhibition
  - Multiple daily doses
- Administered topically
  - Bypasses liver metabolism
  - Enhances commercial viability
Evidence

- Approaching FDA approval for use in dogs
  - Over 8 years of development
**Kinostat**

- **Initial study**
  - 1 drop OU TID
  - 12 placebo dogs
    - 83% developed lens changes in 1 year
    - Complete cataracts in 58%
  - 28 Kinostat treated dogs
    - 46% developed lens changes in 1 year
    - Complete cataracts in 14%
- Safe for use in dogs
Kinostat

![Graph showing cataract scores for Vehicle and Kinostat™ treatments over 0 and 12 months. The graph indicates a statistically significant difference in cataract scores between the two treatments.](image)
Kinostat

- Lens changes? 83% vs 46%
Kinostat

Complete cataract? 58% vs 14%
Kinostat

- Long term study
  - 20 dogs remained on Kinostat
    - 65% never had lens changes (0% complete cataracts)
    - 4 dogs were still enrolled after 5 years with no cataracts
    - 1 dog remains alive 8 years later with no cataracts
BUT...dogs must remain on treatment

- Initial study
  - Participant accidentally taken off
    - Mature cataracts within 2 weeks

- Long term study
  - Participant remained cataract free for 4.5 years
    - Bilateral cataracts within 1 month
  - Smaller lens changes appeared to improve
Kinostat

Recommendation summary

- ALL newly diagnosed diabetic dogs should be placed on Kinostat
- Topical eye drop given three times daily
  - Must be given religiously
  - Commercial availability planned this year
- Kinostat is NOT a treatment for advanced cataracts that are already present
When can we obtain Kinostat?

- Soon to begin testing the mass produced product
- Late 2018
- Are there any options before then?
Maybe...

- Ocuglo

- Antioxidant supplement
  - Grape seed extract, lutein, omega-3 fatty acids, etc

- Shown to delay the onset of diabetic cataracts
  - Average onset of 278 days vs. 77 days in placebo group

- Low numbers, subjective cataract assessment
Keratoconjunctivitis sicca
Keratoconjunctivitis sicca

- Decreased aqueous tear production
  - Immune attack on lacrimal glands
  - Congenitally abnormal lacrimal glands
- Primarily treated with T-cell inhibitors
T-cell inhibitors

- Cyclosporine
  - Isolated from a Norwegian soil fungus in 1972
    - *Tolypocladium inflatum*
    - Optimmune, Restasis
Keratoconjunctivitis sicca

- T-cell inhibitors
  - Tacrolimus
    - Isolated from a Japanese soil bacteria in 1987
      - *Streptomyces tsukubaensis*
      - Protopic
Keratoconjunctivitis sicca

- T-cell inhibitors
  - Cyclosporine
    - Binds to cytophilin receptor
  - Tacrolimus
    - Binds to FK-binding protein
  - Inhibits calcineurin -> prevents T-cell proliferation
Keratoconjunctivitis sicca

- T-cell inhibitors
  - Reduce immune attack on lacrimal glands
  - Stimulate aqueous tear production
  - May lead to regeneration of lacrimal tissue
  - Enhances tear quality
  - Decreases angiogenesis
  - Reduce corneal pigment
Keratoconjunctivitis sicca

- Treatment recommendation
  - Optimmune ointment BID
    - If drop is preferred -> compounded product
    - Can take 2-3 weeks to stimulate (use lubricant)
    - Recheck in 1 month
Treatment recommendation

- Optimmune ineffective?
  - Consider TID
  - OR
  - Consider 2% compounded product
  - OR
  - Start tacrolimus
    - May be more effective in some cases
    - OR
  - Add tacrolimus
    - An additive effect is noted when BOTH are used
Keratoconjunctivitis sicca

- Treatment recommendation
  - Maximum Treatment
    - Cyclosporine 2% TID
    - Tacrolimus 0.03% TID
    - +/- topical steroid BID
Keratoconjunctivitis sicca

- Treatment recommendation
  - Maximum Treatment Fails?
    - Parotid duct transposition
      - Saliva in eye
      - Good Lubrication
      - Issues with calcium deposition
      - Rare issues with discomfort
        - Suspect pH issues
Keratoconjunctivitis sicca

- Tacrolimus 1%
  - NO CURRENT RESEARCH AVAILABLE
Tacrolimus 1%

- Reports of improvement in dogs that are not responding to regular medical management
- My experience: This treatment can improve clinical signs in dogs refractory to other treatments
- At this time: recommended only as a last ditch effort for people trying to avoid a surgery
Keratoconjunctivitis sicca

- Tacrolimus 1%
  - Are there any risks?
Tacrolimus 1%

- Are there any risks?
  - Maybe
Keratoconjunctivitis sicca

- Tacrolimus 1%
  - Are there any risks?
  - ...but it’s a big maybe
Tacrolimus and lymphoma
- Well known to cause lymphoma
  - Chronic, systemic administration (transplant patients)
- Since 2000, topical use for dermatologic disease
  - Here is where the controversy currently stands
Tacrolimus and lymphoma

- Black box warning issued in 2005
  - Initial studies suggested increased risk of cutaneous T cell lymphoma with tacrolimus (8 cases out of 12,000 patients)
  - Increasing use off-label in children under 2 years of age
  - Some felt the warning was issued without enough evidence
  - Issues seen in mice and monkey studies as well
Tacrolimus and lymphoma

- Siegfried et al, 2013 (summary review)
  - Further research has yielded mixed results
  - Current data is inconclusive
    - Lymphoma remains rare
    - Possible relation to systemic dose
Keratoconjunctivitis sicca

- Tacrolimus and lymphoma
  - So what does that mean for us?
    - The systemic dose with other topical medications is low
    - The local dose with 1% is high
    - Lymphoma is rare with dermatologic application
      - No reports exist of a lymphoma attributed to topical ocular tacrolimus use
Tacrolimus and lymphoma

So what does that mean for us?

- Use Tacrolimus 1% only as a last resort
- Inform clients that no research supports the use
- Inform clients that there is a possible risk of lymphoma
Prolapsed Gland of the Nictitans
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Prolapsed Gland of the Nictitans

- “Cherry Eye”
  - Lacrimal gland (~35% of tear production)
  - Weakness of connective tissue attachments
  - Young dogs
  - Beagle, Cocker Spaniel, Lhasa Apso, Pekingese, Bulldog
Prolapsed Gland of the Nictitans

- Surgical repositioning
  - Why not leave it?
    - Chronic irritation, conjunctivitis, keratitis
    - 42.6% of dogs go on to develop KCS (Morgan, 1993)
  - Why not excise it?
    - Excision leads to higher rates of KCS development
Surgical repositioning

Previous options:

- Morgan Pocket technique
- Twitchell technique
- Moore imbrication technique
- Episceral tacking
- Ventral rectus tacking
- Orbital rim tacking
- Nictitans cartilage tacking
Surgical repositioning

Latest approach

- Ventral rectus tacking with cartilage release
- 122 eyes (100 dogs) -> NO recurrences
- My experience -> NO recurrences
  - Two dogs required a second surgery due to gland prominence
Prolapsed Gland of the Nictitans

- Surgical repositioning
  - Ventral rectus tacking with cartilage release
    - Steep learning curve
    - Requires special equipment
    - More difficult in brachiocephalic dogs
    - Quick
Prolapsed Gland of the Nictitans
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Everted Cartilage
Prolapsed Gland of the Nictitans

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Prolapsed Gland of the Nictitans

Everted Cartilage

“Cherry Eye”?

- Abnormal nictitans cartilage shape
  - Congenital
- Young dogs
- St. Bernard, Great Dane, GSD, Weimaraner, Newfandland, Irish Setter, GSP
Everted Cartilage

- Surgical correction
  - Why not leave it?
    - Chronic conjunctivitis with discharge
    - Poor cosmetic appearance
Everted Cartilage

- Surgical correction
  - Previous options
    - Excision of the folded portion
    - Excision and reverse placement of the folded portion
    - Excision and cartilage transplant
  - All work well
    - Instead of better...how about easier and faster!
Everted Cartilage

- Surgical repositioning
  - Latest approach
    - No incisions, no sutures, instant results
    - 12 eyes (10 dogs) -> NO recurrences
    - Concurrent “cherry eye” repaired later
    - My experience -> Not as easy as it looks!

BRIEF COMMUNICATION

Thermal cautery of the canine third eyelid for treatment of cartilage eversion

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Everted Cartilage

- Thermal cautery
  - Start at lowest coagulation setting (NO cutting)
    - Work up from there until effects are seen
  - Light tension with Bishop-Harmon forcep
  - Apply until straight
    - Don’t go too far!
  - Remove any char with a cotton swab
  - Apply to convex surface of scrolled tips
    - Very easy to apply too much power here
Everted Cartilage
Everted Cartilage
Everted Cartilage
Everted Cartilage
Questions?

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