

Ocular Surface Preservation for the Glaucoma Patient.

Prevent Defense is the Best Offense.




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Disclosures

- Speaker- Takeda, Allergan
- Advisory Board- Takeda


Ocular Surface Preservation



What are we looking at? What are we up against?

- DED is one of the most common ocular disease
 - Approximately **30 million** Americans (aprox. 3 million with glaucoma)
- Incidence of OSD increases with **AGE** as well as many other factors
 - DM
 - Migraines
 - Surgery
 - Associated with Anxiety, Depression, and Mental Health Conditions
 - Eye Drops (Blessing or a Curse?) (Gentamicin)
 - Environmental factors including screen time

What are we looking at? What are we up against?




Glaucoma Incidence

- Affects 60 Million Worldwide
- Prevalence increases with AGE
 - 8% of people older than 80

Shares many risk factors with DED

- Age
- DM
- Migraines
- PXP?
- Inflammation?

What are we looking at? What are we up against?



Co-Incidence of OSD and Glaucoma

- The prevalence of OSD is greatly increased in glaucoma patients, reaching 50% of patients in some studies.


Rate of SPK in Glaucoma patients

- As high as 54% of glaucoma patients have SPK

TBUT and Schirmer scores

- Abnormal in >60% of Glaucoma patients

Inflammation and the OSD/Glaucoma Flip-Flop



OSD has longstanding "roots" in inflammation and inflammatory pathways
But what about Glaucoma? Is Glaucoma an inflammatory condition?

- There's a growing body of evidence suggests that neuro-inflammation and immune response are part of the sequence of pathological events leading to the optic neuropathy of glaucoma.
- Azithromycin
 - Strokes, MGD
- Minocycline
 - Strokes, MGD, Corneal Thinning
- Immunomodulation

We Might be treating BOTH conditions when targeting inflammation!!!

Ocular Surface Preservation

TWIN CITIES
OCULAR SURFACE
DISEASE SYMPOSIUM

Glaucoma Therapies and the Ocular Surface

- What are we going to talk about here???

NAME THAT
TUNE

AC/DC
BACK IN BAK

AC/DC
BACK IN BAK

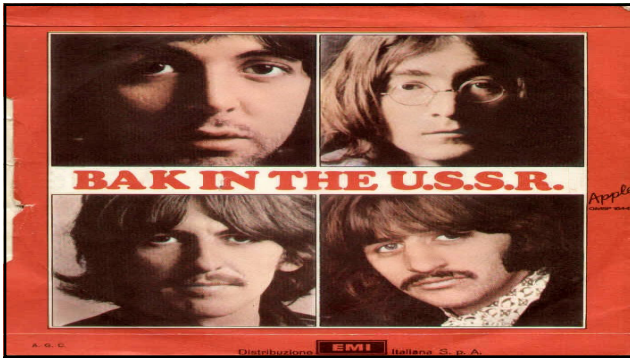
AC/DC
BACK IN BAK

AC/DC
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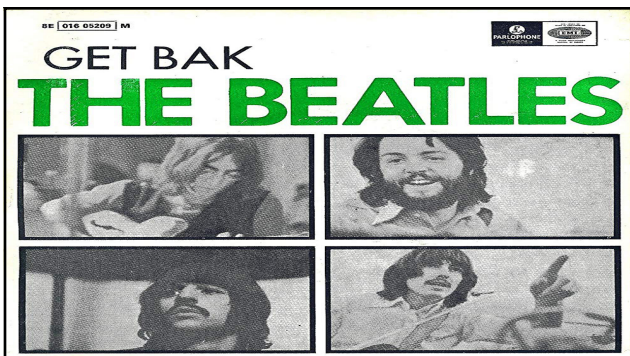








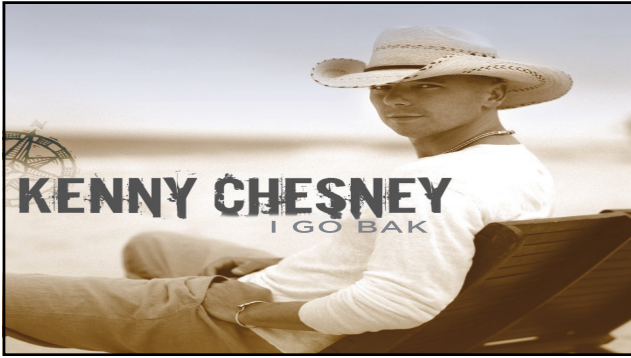








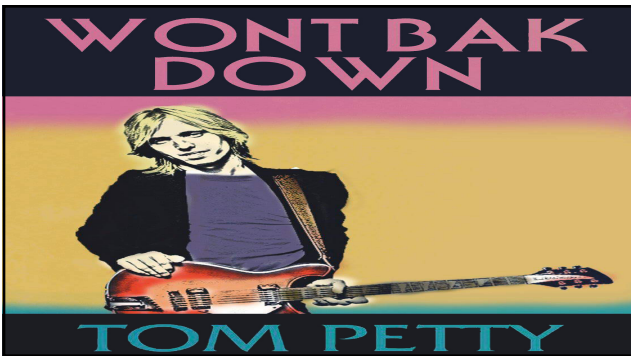














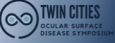


What's the "BAK" Deal? 

(Cue the **BAK** *Rain*, but remember everything is a balance...)

What is **BAK**?


- Quaternary Ammonium Compound
- Bacteriocidal, Bacteriostatic, and surfactant properties
- BAK destroys cell membranes to kill pathogens
- Indiscriminate killer
- BAK exposure is an independent risk factor for DED and OSD
- Has a detergent like effect which destabilizes the lipid layer
- Especially prevalent in generic formulations

What's the "BAK" Deal? 

What is **BAK**?

- BAK has pro-apoptotic effects and causes oxidative stress similar to those found in the TM of glaucoma patients with accelerated aging, trabecular cell death and extracellular matrix accumulation.
- BAK is a lipophilic molecule that accumulates deeply.
- Measurable levels of BAK can be found in the conjunctiva up to 1 week after administration of a single drop.

What's the "BAK" Deal?



What is BAK?

- BAK has been retrieved using the mass spectrometry imaging technique in deep structures such as the **trabecular meshwork** or the **lens** in rabbit eyes treated with BAK for several months, which was also confirmed in human tissues.
- At higher concentrations, sub-conjunctival injection of BAK is capable of causing trabecular cell death, inflammatory infiltration, and **increased IOP**.


Medical Therapies



Prostaglandins

- Known Inflammatory Mediator
- Stimulate the expression of matrix metalloproteinases (**MMPs**) which hydrolyze excessive ECM, opening up extracellular spaces and decrease fluid resistance flowing through these spaces. In addition, they induce relaxation of the TM and ciliary muscle, which reduces tension and increases the outflow pathways.

Medical Therapies



Alpha Agonists

- **Brimonidine**
 - α -2 adrenergic receptor agonist that decreases aqueous humor secretion and enhances aqueous humor resorption by the uveoscleral channels.
 - **Allergenic** and/or pro-inflammatory properties
 - Induces a **Granulomatous Uveitis** (and increased IOP) in some patients
 - Case reports of **INCREASED IOP** with use (inflammatory response?)

Medical Therapies

TWIN CITIES
OCULAR SURFACE
DISEASE SYMPOSIUM

Lumify???



RAUSCH+LOHMANN
LUMIFY
PROSTAGLANDIN ANALOG
ARTIFICIAL TEARS
RELEASING HYPO-OSMOTIC DROPS
• Works in 1 minute
• Lasts up to 8 hours
Sterile 0.08 FL OZ (2.3 mL)

Medical Therapies - Medicamentosa -

TWIN CITIES
OCULAR SURFACE
DISEASE SYMPOSIUM

Medicamentosa

- Allergic manifestations of therapy
 - Hyperemia, chemosis, edema, follicular reaction, etc.
- Prostaglandins 1.5%
- CAIs 3-4%
- Beta-Blockers 11-13%
- Alpha-Agonists 11.5%
 - (Combigan?)

Medical Therapies - Medicamentosa -

TWIN CITIES
OCULAR SURFACE
DISEASE SYMPOSIUM

Medicamentosa

- Pseudopemphigoid
 - Cicatrizing conjunctivitis that mimics true pemphigoid
 - 28.3% of all pseudopemphigoid cases were due to topical glaucoma medications



COVER FOCUS THERAPEUTICS YOU NEED TO KNOW

TABLE. Drugs Commonly Used in the Treatment of Glaucoma

CLASS	GENERIC NAME	TRADE NAME (MANUFACTURER)	MECHANISM OF ACTION	COMMON KNOWN SIDE EFFECTS	NOTES
Prostaglandin Analogues			increases uveo-scleral outflow of fluid from the eye	Eye color change, darkening of eyelid skin, conjunctival redness, dryness of the eyes, eyelid tenderness, and itching	
	latanoprost ophthalmic emulsion 0.005%	Xelpros (Sun Ophthalmics)			BAK-free
	latanoprost ophthalmic solution 0.005%	Xalatan (Pfizer)			Available in generic form
	bimatoprost ophthalmic solution 0.01%	Lumigan (Allergan)			Some formulations available in generic form
	travoprost ophthalmic solution 0.004%	Travatan Z (Novartis)			
	tafluprost ophthalmic solution 0.0015%	Zioptan (Akorn)			BAK-free
	latanoprostene bunod ophthalmic solution 0.024%	Vyzulta (Bausch + Lomb)	increases uveo-scleral and aqueous humor outflow		


TWIN CITIES
OCULAR SURFACE
DISEASE SYMPOSIUM


CLASS	GENERIC NAME	TRADE NAME (MANUFACTURER)	MECHANISM OF ACTION	COMMON KNOWN SIDE EFFECTS	NOTES
Beta Blockers			decreases production of fluid	Low blood pressure, reduced pulse rate, fatigue, shortness of breath	Second most often used class of medication
	timolol maleate ophthalmic solution	Timoptic 0.25% and 0.5% (Bausch + Lomb)			Available in generic and preservative-free formulations
Alpha-Adrenergic Agonists			decreases production of fluid and increases drainage	Burning or stinging, fatigue, headache, drowsiness, dry mouth and nose, higher likelihood of allergic reaction	
	brimonidine tartrate ophthalmic solution 0.2%	Alphagan (Allergan)			Preserved in BAK; available in generic form
	brimonidine tartrate ophthalmic solution 0.1% or 0.15%	Alphagan P (Allergan)			Preserved in stabilized oxychloro complex (Purite Allergan)


TWIN CITIES
OCULAR SURFACE
DISEASE SYMPOSIUM

Medical Therapies

CLASS	GENERIC NAME	TRADE NAME (MANUFACTURER)	MECHANISM OF ACTION	COMMON KNOWN SIDE EFFECTS	NOTES
Miotics			increases outflow	Blurred or dim vision, headache, redness of eyelids, tearing or swelling of the eye, itching or redness of the eye, stinging, burning, or discomfort in the eye	
	pilocarpine HCl ophthalmic solution 1%, 2% and 4%	Isopto Carpine (Alcon)			Preserved with BAK; available in generic form
	pilocarpine HCl ophthalmic gel 4%	Pilopine HS (Alcon)			Gel formulation

Medical Therapies					
					
CLASS	GENERIC NAME	TRADE NAME (MANUFACTURER)	MECHANISM OF ACTION	COMMON KNOWN SIDE EFFECTS	NOTES
Combination Agents					
	dorzolamide HCl 1%/timolol maleate 0.5% sterile ophthalmic solution	Cosopt (Akorn)			Available in generic form and as a preservative-free formulation
	brimonidine tartrate 0.2%/timolol maleate ophthalmic solution 0.5%	Combigan (Allergan)			
	brinzolamide 1%/brimonidine tartrate ophthalmic suspension 0.2%	Simbrinza (Alcon)			Includes no beta blocker

Medical Therapies					
					
CLASS	GENERIC NAME	TRADE NAME (MANUFACTURER)	MECHANISM OF ACTION	COMMON KNOWN SIDE EFFECTS	NOTES
Carbonic Anhydrase Inhibitors, Topical					
	dorzolamide ophthalmic solution 2%	Trusopt (Santen)	decreases aqueous production	Stinging, burning, eye discomfort	Available in generic form
	brinzolamide ophthalmic suspension 1%	Azopt (Alcon)			

Medical Therapies					
					
CLASS	GENERIC NAME	TRADE NAME (MANUFACTURER)	MECHANISM OF ACTION	COMMON KNOWN SIDE EFFECTS	NOTES
Carbonic Anhydrase Inhibitors, Oral					
	acetazolamide 125 mg to 250 mg		decreases aqueous production	Tingling hands and feet, fatigue, upset stomach, memory problems, frequent urination	Available in generic form
	acetazolamide 500 mg				Available in generic form
	methazolamide 25 mg and 50 mg				Available in generic form
	dichlorphenamide 50 mg	Keveyis (Strongbridge Biopharma)			

Medical Therapies

CLASS	GENERIC NAME	TRADE NAME (MANUFACTURER)	MECHANISM OF ACTION	COMMON KNOWN SIDE EFFECTS	NOTES
Rho Kinase Inhibitors	Netarsudil ophthalmic solution 0.02%	Rhopressa (Aerie Pharmaceuticals)	increases drainage of aqueous	Eye redness, corneal deposits, stinging, and small scleral bleeds	

Medical Therapies

TABLE 2. COMMONLY PRESCRIBED GLAUCOMA MEDICATIONS WITH THEIR CORRESPONDING PRESERVATIVE*

Medication	Preservative
Xalatan	BAK 0.02%
Lumigan	BAK 0.02%
Azopt	BAK 0.01%
Timoptic	BAK 0.01%
Truopt	BAK 0.0075%
Cocept	BAK 0.0075%
Combigan	BAK 0.005%
Travatan Z	SoFzia
Alphagan P	Purite
Zipscan	None
Cocept PF	None
Timoptic in Ocusite	None

Vyzulta 0.02% BAK
Rhopressa 0.015% BAK
Simbrinza 0.003% BAK


IOP-Lowering medications	BAK concentration %
Xalatan	0.02
Travatan	0.015
Betoptic S	0.01
Azopt	0.01
Timoptic	0.01
Simbrinza	0.003
Brimonidine	0.005
Lumigan	0.005
Betagan	0.005
Combigan	0.005
Cocept	0.0075
Truopt	0.0075

Preservative-Free Alternatives
Options for decreasing ocular toxicity in patients with glaucoma
*Preservative-Free Alternatives: Ocular Surface Disease Symposium


Tear Osmolarity in a Glaucoma Practice
The role of point-of-care testing in dry eye disease and glaucoma management
*Tear Osmolarity in a Glaucoma Practice: Ocular Surface Disease Symposium

Ocular Surface VS. Optic Nerve Testing

- What do you **do** when you see a patient with Glaucomatous Optic Neuropathy???
- What do you **do** when you see a patient on Plaquenil?
- How do you **track** the effectiveness of your therapy?
- How do you know there's been a **change** without a **baseline**?
- Do you tell refractive surgery patients that it may **worsen** their OSD?

Ocular Surface VS. Optic Nerve Testing 

Contents lists available at ScienceDirect


 **The Ocular Surface**
journal homepage: www.theocularsurface.com

Original Research


Exploring topical anti-glaucoma medication effects on the ocular surface in the context of the current understanding of dry eye

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Department of Ophthalmology, New Zealand National Eye Centre, The University of Auckland, New Zealand

Ocular Surface and Medical Glaucoma Tx 

- Of note, **decreased tear film stability** and **elevated tear osmolarity**, both global indices of dry eye disease, were observed in eyes treated with topical anti-glaucoma medications.
- This was associated with **increased levels of bulbar conjunctival hyperemia** and **eyelid margin changes**.
- These findings suggest that **inflammatory mechanisms** may play a role in the propensity of dry eye development in patients receiving long term topical anti-glaucoma medications.


Baseline DED/OSD Testing 

- Osmolarity
- Inflammation
- Staining
 - Fluorescein,
 - Lissamine green
- Tear Prism
- Tear Production
 - Schirmer
- TBUT
- Symptom Surveys
 - SPEED
 - DEQ-5
- Meibography & Gland Analysis/Expression
- Lid Anatomy, Skin Conditions, Demodex

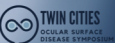
OSD Treatment in the setting of Glaucoma 

Influence of Treating Ocular Surface Disease on Intraocular Pressure in Glaucoma Patients Intolerant to Their Topical Treatments: A Report of 10 Cases


Pierre Dubrulle, MD† Antoine Labbé, MD, PhD,*†‡§
Emmanuelle Brasnu, MD, PhD,* Hong Liang, MD, PhD,*†‡
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and Christophe Baudouin, MD, PhD*†‡§*

DED Treatment in the setting of Glaucoma 

- Case Series of patients referred for filtering glaucoma surgery.
- The main treatments were change of topical anti-glaucoma medications to preservative-free equivalents, removal of allergenic treatments or those identified as causing side effects, switch to another therapeutic class with the same efficacy but with a better safety profile .
- Treatment of OSD, especially MGD.


DED Treatment in the setting of Glaucoma 

- After a minimum follow-up of 6 months, we observed improved ocular surface in all patients, associated with an intraocular pressure (IOP) decrease or stabilization even if some anti-glaucoma medications were removed. The mean IOP significantly decreased from 23.75±9.98mmHg to 15.15±4.75mmHg (-36.2%; P=0.0001). The mean number of IOP-lowering medications was 3.7±1.06 at presentation and 2.8±0.63 after treatment (P=0.01). The Oxford staining score also decreased from a mean 1.7±0.67 to 0.4±0.51 (-76.5%; P<0.001).
- For 2 patients, IOP was not sufficiently reduced after treatment and they finally underwent filtering surgery.
- You need surgery? PROVE IT!
- Who wants to do surgery on a sick ocular surface?

DED Treatment in the setting of Glaucoma 


Decrease Inflammation

- Decrease **BAK** (other preservatives) Load
- Anti-Inflammatory Medications
 - Lofitagrast
 - Cyclosporine
 - NSAIDS
 - Acuvail is **PF**
 - Steroids
 - Nanoparticles

DED Treatment in the setting of Glaucoma 


Decrease Inflammation

- Tear Stimulation
 - **TrueTear**
- **"Fill" the Swamp?** (Plugs)
- Treat the Lids
 - Lipiflow, iLux, TearCare
 - Lid Hygiene
 - IPL
- Don't forget about
 - Contact Lens Care & Solutions
 - Allergic Conjunctivitis

DED Treatment in the setting of Glaucoma 

Decrease Inflammation

- Medication Vacation
 - Oral CAIs as a transitional therapy


DED Treatment in the setting of Glaucoma 

What about **Punctal Plugs**?

Effect of a punctal plug on ocular surface disease in patients using topical prostaglandin analogues: a randomized controlled trial

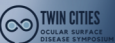
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DED Treatment in the setting of Glaucoma 

What about **Punctal Plugs**?


- Conclusions and Relevance: Punctal plug insertion improves **subjective and objective measures of OSD** and results in a **reduced IOP** in patients with symptomatic ocular surface disease using prostaglandin analogue monotherapy.
- TBUT **increased**
- Oxford Staining Score **decreased**
- Tear Osmolarity **decreased**

DED Treatment in the setting of Glaucoma 

What about **Surgery**?

- SLT and MIGS
 - Should SLT be the **first option** for POAG with concomitant OSD???
- At Cataract Extraction
 - PHACO Study
- Filtering procedures (Trabs and Tubes)
 - What is the **first/most important** intra-operative indicator of success

THANK YOU!



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Slide Magician

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NAME THAT
TUNE


oasis

DON'T LOOK BAK IN ANGER











Additional Reading

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