Women of Vision Present
“When Treatment and Disease Come Full Circle”

Lifestyle issues and medical therapy can affect our management of ocular disease such as glaucoma and ocular surface disease. Join this panel as we discuss the relationship of headaches, sleep apnea, and the undesired side effects of our treatments for these common eye conditions.

Women of Vision Present
“When Treatment and Disease Come Full Circle”

Louise Sclafani OD, FAAO
Leslie O’Dell, OD, FAAO
Katherine Mastrota, MS, OD, FAAO

“When Treatment and Disease Come Full Circle”

Discuss the cosmetic and OSD effects of glaucoma medications
Treatment considerations for the patient with both glaucoma and OSD
Discuss the relationship between sleep apnea, headaches and OSD
Discuss lifestyle issues such as obesity, alcohol, smoking, sleep apnea and dental hygiene and relationship to glaucoma.
Gender and Glaucoma: What we Know and What We Need to Know

“Current evidence suggests that older women are at risk for glaucoma and glaucoma blindness. Further interdisciplinary research involving investigators, specialized in glaucoma, women’s health and health disparities, will lead to better understanding of gender health disparities in glaucoma and better targeting populations at risk”

Vajaranant TS, Nayak S, Wilensky JT, Joslin CE

LIFESTYLE CONSIDERATIONS THAT MAY EFFECT IOP and it’s TREATMENT

- Systemic and Ocular Medications
- Age
- Sex
- Physical Activities: Yoga, Golf, Aerobic, Sex
- Hobbies: Musical Instruments, Fashion
- Sleep Apnea
- Coffee and Alcohol intake
- Smoking: Tobacco, Marijuana
- Weight
- Sleep Habits
- Oral Health
- Vitamin supplements
- Dry Eye
Poor Oral Health May be Associated with Primary Open Angle Glaucoma

- Previous studies showed glaucoma patients had higher bacterial load and less teeth (Hyman et al).
- Poor oral health associated with impaired blood flow, endothelial dysfunction
  - DM, CVDx, RA
- N > 49K Men 1986-2012
- 485 confirmed GLC cases

**RESULTS**

- Loss of 1 or more tooth in past 2 years had 45% chance of POAG
- Loss of 1 or more tooth and periodontal dx in past 2 years had 85% chance
- More para-central VF loss (impaired blood flow)


Smoking And Incidence of Glaucoma

The SUN Cohort

- 1.3 B smokers/world
- Smoking/oxidative stress...TM/RGC damage
- Prospective, dynamic study, Spain, multipurpose
- Previous Studies ???
- N = 16,797, Non-GLC FU= 8.5 years, 1999 ongoing
  - Biennial Questionnaire
  - Diet/social
  - # pack yrs/Passive

**RESULTS**

- 7920 NS, 5160 S, 3729 PS
- Smokers more likely to drink coffee/ETOH, HTN/DM, and Med diet.
- 184 new diagnosis
- Direct Association between current smokers and glaucoma DDX (1.8x)
- + Dose response
  - 70% higher risk > 20 pack
- PS = non- significant higher risk

Monica Perez-de-Arcelus et al Medicine (2017) 96:1

THEORIES About SMOKING & GLAUCOMA

- Smoking causes oxidative stress
- Leads to apoptosis...TM and RGC death
- Smoking alters biosynthesis of collagen
- Leads to corneal thinning
- Smoking causes vasoconstriction
- Epi-scleral constriction reduces aqueous outflow
- Smoking causes inflammation
- Can contribute to progression
Leslie E. O’Dell OD, FAAO

- Consulting/Speaker
- Aerie Pharmaceutical
- Shire
- Paragon BioTeck
- Allergan

Director of The Dry Eye Center of PA at Wheatlyn Eye Care
Manchester, PA
TFOS DEWS II Public Awareness Committee Member

Glaucoma and Ocular Surface Disease
Leslie E. O’Dell OD FAAO

1st line treatment- Glaucoma

- Glaucoma is often asymptomatic to the patient – until you start therapy
- Understand the ocular surface of the patient BEFORE you initiate treatment
- Monitor the ocular surface during glaucoma management
- Understand the side effects of the Prostaglandin Analogues
Dry Eye Disease Defined

- Tear Film and Ocular Surface Society’s Dry Eye Workshop in 2007 defined dry eye as the following:
  - A multifactorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbance, and tear film instability with potential damage to the ocular surface. It is accompanied by increased osmolarity of the tear film and inflammation of the ocular surface.

5. TFOS DEWS II – updated definition – ARVO May 2017

Dry eye – a growing concern

- TFOS DEWS II release early 2017 www.tearfilm.org
- F>M
- More prevalent with age and lack of adequate treatment
- Exacerbated by intense and prolonged visual tasks
- Impacts contact lens wearers and surgical outcomes
- Exacerbated by PROLONGED exposure to preservatives - mainly BAK
### Incidence of DED and Glaucoma patients

- Jaenen et al., 2007
  - Stinging or burning 47.5%
  - Foreign body sensation 41.9%
  - Dry eye sensation 34.9% of patients using preserved glaucoma medications
- Fechtner et al., 2010
  - Using OSDI – 40-59% of glaucoma patients had dry eye symptoms
- Baudouin et al., 2012
  - 516 patient on topical antiglaucoma therapy
  - Burning (47.3%), eye dryness (44.0%), foreign body sensation (39.9%), itching (38.1%), tearing (31.6%)
  - Conjunctival hyperemia (60.3%), eyelid margin redness (46.7%)
  - Corneal staining (34.7%) or conjunctival staining (28.3%)
  - Decreased tear break up time (TBUT) below 5 seconds (20.9%)

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### Iatrogenic

- **i·at·ro·gen·ic**
  - adjective
  - relating to illness caused by medical examination or treatment

### Dry Eye Disease

- Topical anti-glaucoma therapies
- Perservatives -- BAK

### Risk Factors:

- Underlying risk factors -- age/sex/medication
- Number of BAK containing medications
- Dosing schedule of BAK containing medications
- Years on therapy

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### Drug Components

- Active drug
- Preservative
- Drug delivery system
- Viscosity-increasing agents
- Buffers and stabilizers
- Carrier vehicle

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BAK - the corneal killer

• Role of BAK:
  - A quaternary ammonium compound, a detergent that disrupts cell membranes leading to cell death and increased permeability
  - Ranges in concentration from 0.004%-0.02%
  - Prevents contamination
  - Increased penetrance of drug

• Long term risks:
  - Disruption of HOMEOSTASIS – stripping oil from the outer lipid layer — accelerated evaporation and tear film instability

40% of Medications in Use ≥9 Weeks Are Contaminated

<table>
<thead>
<tr>
<th>Time in Use (weeks)</th>
<th>Tested No.</th>
<th>Medications Contaminated No. (%)</th>
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<tbody>
<tr>
<td>&lt;4</td>
<td>108</td>
<td>20 (19)</td>
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<tr>
<td>5-8</td>
<td>44</td>
<td>9 (20)</td>
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<tr>
<td>9-12</td>
<td>17</td>
<td>7 (41)</td>
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<tr>
<td>&gt;12</td>
<td>25</td>
<td>10 (40)</td>
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The Preservative Burden

• The number of medications correlates to DED
  - 39% 2 drugs
  - 43% 3 drugs
  - 11% 1 drug

<table>
<thead>
<tr>
<th>Medication</th>
<th>% BAK</th>
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<tbody>
<tr>
<td>Xalatan</td>
<td>0.02</td>
</tr>
<tr>
<td>Travatan</td>
<td>0.015</td>
</tr>
<tr>
<td>Betoptic S</td>
<td>0.01</td>
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<tr>
<td>Azopt</td>
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<tr>
<td>Timoptic</td>
<td>0.01</td>
</tr>
<tr>
<td>Simbrinza</td>
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<tr>
<td>Brimonidine</td>
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<tr>
<td>Lumigan</td>
<td>0.005</td>
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<tr>
<td>Betagan</td>
<td>0.005</td>
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<tr>
<td>Combigan</td>
<td>0.005</td>
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<tr>
<td>Cosopt</td>
<td>0.0075</td>
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<tr>
<td>Trusopt</td>
<td>0.0075</td>
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</table>
Preservative Free and alternate options

<table>
<thead>
<tr>
<th>Preservative Free</th>
<th>Alternate preservative</th>
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<tr>
<td>Zioptan</td>
<td>Travatan Z, Sofzia</td>
</tr>
<tr>
<td>Cosopt PF</td>
<td>Alphagan P, Purite</td>
</tr>
<tr>
<td>Timoptic in Ocudose</td>
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</tbody>
</table>

Ocular Surface under attack

- Targets of topical therapies:
  - Tear Film
  - Conjunctival epithelium
  - Corneal epithelium
  - Corneal nerves
  - Eyelid margin keratinization – Meibomian glands
  - Corneal Keratitis (Gobbels and Spitznas, 1992)
  - Reduced Goblet Cell Density (Herreras et al., 1992)
  - Fibroblast proliferation
  - Neurotoxic effects (Barkar et al., 2012), (Baudouin et al., 2013)
  - Future surgical complication
  - Cataract formation

First line treatment Options: GLAUCOMA

- Medication
  - Class of medication
  - Preservative?
  - Preservative free
- SLT
When choosing a topical therapy

- Class of drug
  - Beta Blockers
    - Shown to decreased tear production
- Cosmetic side effects
  - Prostaglandin Associated Periorbitopathy (PAP)

The not so pretty side of PGAs

- Periorbital fat cell atrophy
- Ptosis
- Hyperemia of lid margin

What’s hiding in the lid

- J Glaucoma 2016
- Long-term administration of PGA is associated with obstructive type of MGD
- 70 patients (70 eyes)
- Obstructive type of MGD was detected in the majority of patients treated with PGAs (95.7%)
- Grade 2 and 3 MGD was noted in 80.5% of patients on PGA
- Patients on PGA had worse ocular surface disease index and ocular surface test results (P<0.001) compared with those of control subjects
Treatment without topicals

- Improved compliance
- Improved costs to patient
- Improve ocular surface
- Repeatable treatments
- When adjunct therapy need to reduce the preservative load on the ocular surface
  - as many as 40% of patients need more than one medication

Topical vs. Selective Laser Trabeculoplasty

- Achieving target IOP with SLT
  - SLT is effective around 80 percent of the time and that it lowers IOP by 20-25%
  - SLT/MED study found similar efficacy between SLT topical
- Achieving target IOP with 1 topical medication
  - Monotherapy timolol can lower IOP by 25%
  - PGA's can lower IOP 6-8 mmHg

Making the Switch

- Pisella et al., 2002.
  - The change from preserved to non-preserved 161 glaucoma medications significantly reduced
    - discomfort upon instillation (43% vs. 17%)
    - burning/stinging (40% vs. 22%)
    - FB sensation (31% vs. 14%)
    - dry eye sensation (23% vs. 14%)
    - tearing (21% vs. .14%)
    - eyelid itching (18% vs. 10%)

Evaluate for DED prior to treatment of Glaucoma

- HPI/Symptoms review
- Oral medication risks
- Exam
- Point of care testing

Point of Care Testing in a glaucoma practice

- Point of care testing allows for collection of data from a patient’s tear film much like management of glaucoma more data points helps make a solid diagnosis and improves treatment outcomes
- CLIA license
- Current Diagnostics:
  - Osmolarity - Tear Lab
  - InflammaDry - RPS

BAK and osmolarity

- Hyperosmolarity
  - A recent study showed by switching patients from a BAK-containing prostaglandin to tafluprost once daily mean tear osmolarity decreased significantly over a 12 week period
  - Decrease in osmolarity from baseline of 315.7 mOsms/L to 302.0 mOsms/L
  - Improving osmolarity for 81.7% of the patients
Glaucoma and MGD are both diagnosed and managed with the framework of Function and Structure due to the introduction and evolution of metrics.

The NFL of the anterior segment?

Rethinking glaucoma management

- If DED is present – start Preservative Free
- If DED is absent – evaluate options, think preventative and consider alternate preservatives to start
- If DED develops- change treatment modality
- Consider the unwanted side effects of PGA – especially for your “cosmetic conscious” patients
Coming Full Circle

- Change the way we treat our glaucoma patients
- Evaluate the ocular surface at every exam
- If DED:
  - Change treatment – preservative change or preservative free options
  - Treat DED aggressively

Importance of sleep for wellness

- NIH states adults need 7-9 hours per night
- Proper sleep is associated with
  - Lower risk of obesity (abdominal), DM2, HTN
  - Better nutrient profiles
  - Higher adiponectin levels and Lower ghrelin levels
  - Produced while asleep: helps burn fat & control hunger
- Less sleep = Less Energy
  - Need to eat more but poor choice
  - Less energy for physical activity
  - Growth hormones effected: Muscle building, repairing and rejuvenating tissue is impaired. Lowers metabolism resulting in less muscle and more fat.

Orfeu Buxton at Brigham and Women's Hospital

Lack of sleep effects body's rhythm with physical changes

- Less than 5 hours is harmful
- N= 21, Healthy volunteers, monitored for 6 weeks
- Allowed only 5 ½ hours sleep q 24 hours
- B.S. levels increased after meals, pancreas stopped secreting enough insulin, pre-DM levels
- Metabolic rate slowed by 8%
  - (≈ 10-12 lbs/year)
- Took 9 nights of normal sleep to return to baseline
- ? For permanent damage

Orfeu Buxton at Brigham and Women's Hospital
“Sleep is the enemy of capitalism”

- You can’t produce or consume while asleep!
- Technology interrupts our natural rhythm
  - Time spent on instruments erase boundaries of time
  - Blue λ suppress melatonin
  - Night shift-workers wear yellow-orange tints on way home
  - Carcinogen? Light at pm may hamper tumor suppressor cells
  - Treat sleep apnea!
- Hypersomnia: > 12 hours
  - Diminished Return: groggy during the day, more naps!
  - Find root cause: associated with thyroid, kidney and liver disease, depression and dementia

Russell Sanna, Harvard Medical School

Katherine M. Mastrota, MS, OD, FAAO

Consulting/Speaker
- Allergan
- B+L
- BioTissue
- Paragon BioTeck
- Science Based Health
- Shire
- Valeant

Director of Optometry
The New York Hotel Trades Council
Employee Benefits Fund Health Center, Inc
The Hotel Association of New York City, Inc
Diplomate, American Board of Optometry

Sleep, Sleep Apnea, Headaches and Ocular Surface disease

Katherine M. Mastrota, MS, OD, FAAO
Sleep

Sleep that knits up the ravel'd sleave of care,
the death of each day's life,
sore labour's bath,
balm of hurt minds,
great nature's second course,
chief nourisher in life's feast.

William Shakespeare, Macbeth, Act II, sc. 2

Sleep Disorders

- Dyssomnias (insomnia, hypersomnia, sleep apnea)
- Parasomnias (sleepwalking, REM behavior disorder)
- Bruxism
- Circadian rhythm sleep disorders

Sleep, Sleep Apnea, HAs and OSD
OSA: Cessation of air flow > 10 seconds

Risk Factors
- Obesity
- Increased age
- Male
- Thyroidism
- Acromegaly
- Use of sedatives/alcohol/narcotics
- Smoking
- Family history of OSA

- Smoking
- Increased parapharyngeal fat (neck >17" men, 16" woman)
- Tonsillar hypertrophy
- Macroglossia
- Microstomia
- Long soft palate
- Enlarged adenoids

OSA: 80-90% Under-diagnosed

Symptoms
- Snoring
- Choking/gasping during sleep
- Restless sleep
- Insomnia
- Nocturia

- Morning nausea
- Impaired concentration
- Memory impairment
- Depression
- Impotence
- Personality changes
- Morning headache

OSA

Medical
- Hypertension
- Cardiac arrhythmias
- Myocardial infarction
- Congestive heart failure
- Stroke
- Angina
- Depression
- Type II diabetes

29.4 Million Americans
- 149 Billion economic cost
- Most OSA undiagnosed
- Epworth Sleepiness Scale
OSA and the (Dry) Eye
- Asthenopia
- CPAP-related ocular surface challenges
- FES
- Low-tension glaucoma
- NAION
- Papilledema

**2016, from Japan, sleep quality is associated with DED: sleep disturbance influences DED, especially on dry eye symptoms.**

FLOPPY EYELID SYNDROME

OSA, Sleep, and the (Dry) Eye
- FES and OSA
- Sleep posture may be a factor in OSD
- Sleep disturbance is a common non-motor phenomenon in Parkinson's disease
OSA, Sleep, and the (Dry) Eye

The CDC recognizes insufficient/poor sleep as a public health problem.

This begs the question: Should we incorporate a validated sleep survey into our dry eye exams?

Sleep, HAs and Dry Eye

Insufficient sleep is prevalent among migraines: a population-based study

Dry eyes and migraines: is there really a correlation?
Beaver Dam Offspring Study

- An association was found between report of migraine headaches and dry eye symptoms.

- Dry Eye in the Beaver Dam Offspring Study: Prevalence, Risk Factors, and Health-Related Quality of Life
  Adam J. Paulsen,1 Karen J. Cruickshanks,1,2
  Mary E. Fischer,1 Guan-Hua Huang,3 Barbara E. K. Klein,1 Ronald Klein,1 and
  Dayna S. Dalton1

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TRAVEL INDUSTRY puts great emphasis on sleep

- Set your thermostat between 68-72 degrees
- Lower lights and sound 1 hour before sleep to trigger body to start producing melatonin
- Put cell phone and alarm clock in drawer (masks)
- Don’t eat, work-out or drink 3 hours prior
- Avoid anxiety triggers (emails, news) etc..
- Noise cancellation headphones
- Various mattresses firmness
- Essential oils-Lavender
Continuous IOP Monitoring during Nocturnal Sleep in Patients with Obstructive Sleep Apnea Syndrome

- OSA affects up to 20%
- Correlates with obesity, males, respiratory track abnormality, thick neck, snoring and increased ETOH
- Evaluate IOP changes during nocturnal sleep using CL sensor
- Prospective cohort study
- KKK Sapporo Medical Center
- N=7 (25%) + OSAS, - Ocular dx.
- All Overweight, Mean BMI 31
- SENSIMED Trigger Fish


SMART LENSES

Wireless Technology to keep an "eye" on health

SENSIMED TRIGGER FISH Detects
curvature changes reflecting IOP changes
during 24 hour period.
- Every 5 minutes/30s/288 per day
- Measure mVeq

Replace blood test by checking bio-
markers in tears for cholesterol, sodium,
potassium, glucose
Continuous IOP Monitoring during Nocturnal Sleep in Patients with Obstructive Sleep Apnea Syndrome

O2 levels in tissue decrease significantly in OSA, esp. REM
Associated with Flapery, KCN, PAPEdema, NAKIN, Glaucoma

RESULTS
7 had Severe OSA (>30 AHI)
O2 Saturation 76-95%
IOP levels significantly declined in immediate response to apnea events

Valsava = contraction
+ Intrathoracic venous Pressure
Increases IOP
Viera et al - Bench press study (wind instruments)
Muller = inspiration against obstruction
-Intrathoracic venous Pressure
Decreases IOP
Pepin et al, • airway TX • nocturnal IOP


Caffeine Consumption and the Risk of Primary Open Angle Glaucoma

• Coffee causes transient increase in IOP of 2mmHg for 2 hr. period
• 80% of >50 consume
• Prospective Cohort
• N = > 100K M/F from 1980-2004
• Biennial Q
• Glaucoma N = 1011

RESULTS
Overall caffeine intake was not associated with increased risk of POAG
Caffeine 5+ cups appeared to elevate risk of POAG in patients with FoHx
• Concern that caffeine decreases blood flow to ONH and macula
• Inverse relationship w/ leaf
• Flavonoids?

Kang et al. IOVS 2008 May;49 (5)

Prospective Study of Alcohol Consumption and the Risk of Primary Open Angle Glaucoma

• Alcohol reduces IOP
• Large, prospective
• 1980-2002 M/F >40 y
• Non- Glaucoma
• Q for self-reported new diagnosis of glaucoma
• Controlled for other factors

RESULTS
Alcohol consumption < 30 g/day did not influence POAG risk compared to non-drinkers

Kang et al. Ophthalmic Epidemiology, 2007 May-June;14 (3):141-7
Thank you for your attention
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