Sleep Apnea and the Eye

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Types of Sleep Apnea

Central Sleep Apnea (.4%)
Obstructive Sleep Apnea (OSA). 84%
Mixed (15%)

Apnea is Greek word meaning "without breath"
Needs to be part of history

Obstructive Sleep Apnea

Soft tissues of the throat collapse and occlude airway
Happens continually during sleep cycle
Occlusion of airway leads to decreased blood oxygen
Brain then signals body to "wake up" and breathe

Central Sleep Apnea

Break in respiratory effort
Improper central command
Uncommon
Known as Cheyne-Stokes syndrome

OSA

Most common in overweight / obese men
Gasping episodes
Snoring very common
Symptoms of daytime sleepiness
Cognition problems
Restless sleep, morning headaches
“Pickwickian Syndrome”

Comes from the “fat boy” character in Charles Dickens novel “The Pickwick Papers”

Refers to the character traits and general habitus of OSA patients

OSA

Each pause in breathing is an “apnea”. Last seconds to minutes

Each low breathing event is called a hypopnea

Risk factors include obesity, age, male, smoking, neck circumference over 48 cm (19 inches)

Signs and Risks

- Snoring
- Tiredness
- Observed stop in breathing
- Pressure (increased BP)
- BMI
- Age (>50)
- Neck Size (19 inches)
- Gender (Male)

OSA

Very, very sensitive sign………

Snoring that stops

- Sleeping partners aware
- Sufferer almost never aware during sleep, but experiences associated problems during the day

OSA systemic complications

Heart disease

Hypertension (due to increased epinephrine and norepinephrine production)

HTN induced by sleep apnea does not decrease with sleep

Stroke and atrial fibrillation

Increased LDL, triglycerides, and total cholesterol; decreased HDL

2 x incidence of gout

Interestingly, OSA patients who have a non-fatal heart attack often have less residual damage.

Perhaps their tissue is more used to ischemia from chronic poor oxygen delivery.
OSA statistics

Incidence varies widely in the literature
High end of up to 24% of M and 9% of F
80% of men and 90% of women with OSA are undiagnosed
Only 10% of people with OSA are actually treated
70% of obese individuals have OSA
50% of heart disease patients have OSA
72% of stroke patients have sleep apnea!!!!!!! (meta analysis of 29 studies and well over 2000 patients)
80% of patients with difficult to control hypertension have OSA
African Americans at 2.5 X risk
High incidence in psychiatric populations
And most importantly.........34% of NFL Linemans have OSA!

Cancer and OSA

April 2014 issue of the Journal of Clinical Sleep Medicine
Patients with OSA followed for 20 years had, compared to normals............
Cancer incidence was 2.5 X higher with OSA
Cancer mortality was 3.4 X higher

Mortality and OSA

2015 study of over 3 million US veterans (93% male)
Untreated OSA = 86% higher mortality risk compared to non-OSA
CPAP treated OSA = 35% higher mortality risk compared to non-OSA

Diagnosis of OSA

Epworth sleepiness scale
Uses self report of likelihood of falling asleep during separate activities
0 = unlikely
1 = slight
2 = moderate
3 = high
Scored on a scale up to 24 points

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Diagnosis of OSA

Pulse oximetry
Performed at home
Measures blood oxygen levels at various times during the night
Low blood oxygen is called hypoxemia

Gold standard is Polysomnography sleep study
Inconvenient and problematic for many patients because they must stay overnight
“Hooked up” to a large number of machines

Diagnosis of OSA

Sleep study order IU Health

Prices at different facilities range from $3000.00 to $5000.00
Small false negative rate with single night test: about 3%

Diagnosis of OSA

AHI= Apnea Hypopnea Index
RDI = Respiratory Disturbance Index
5-15 events per hour = mild OSA
15-30 = Moderate OSA
> 30 = Severe OSA

Home testing devices starting to gain favor. Driven by insurance carriers due to cost of PSG. About $800

Treatment options for OSA

Lose weight!
Stop smoking
Avoid alcohol
Avoid sleeping pills
Sleep on side
Acetazolamide (lowers blood PH and encourages respiration)

Dental appliances (OAT)
Move lower jaw forward to keep airway open
Makes TMJ worse!
75% effective in mild and moderate OSA

Treatment options for OSA

Pillar procedure
Performed in office with anesthetic and syringes
Inserts Dacron strips into soft palate to keep airway open
Treatment options for OSA

**CPAP**
Continuous Positive Airway Pressure
A machine and mask combine to provide a continuous flow of air to “force” airway open
Amount is titrated, but continuous

**When CPAP does not work**

Auto titrating CPAP
Continually adjusts flow pressure automatically

BiPAP
Delivers higher dosing, and has a different pressure between inhaling and exhaling

For both, usually must try CPAP first (insurance)

Treatment options for OSA

Many different manufacturers of “machines” and “masks”
Masks can be nasal or more full face
Less than 50% of people stick with therapy

Uncomfortable
Noisy
Difficult when traveling
No “point of use” satisfaction

Surgical options for OSA

Maxillo-Mandibular Advancement (MMA)
Uvulopalatopharyngoplasty (UPPP)
Tongue reduction surgery (seriously!)

Some newer options........

1) Provent: band-aid like device covering each nostril with center valve creating pressure. $70 per one month supply
2) Winx: Small mouthpiece that rests inside the mouth and creates suction to open airway. $700
3) Inspire upper airway stimulation: stimulates nerves to keep airway open. Surgical procedure. FDA approved but insurance concerns. Can’t do if BMI over 32

Potential New Drug

Dronabinol
A synthetic cannabis / THC compound
Positive results in phase 2 trials
Jury is out until larger phase 3 trials are conducted

Would be the first pharmaceutical agent specifically for OSA
Alternative treatment for OSA

- Playing the didgeridoo!
- Strengthens muscles in the throat thus preventing night time collapse
- Proven effective in a 2005 study in the British Journal of Medicine

Ocular Side effects of OSA

- Floppy Eyelid Syndrome (FES)
- Keratoconus
- NAION
- Glaucoma, especially NTG
- Papilledema
- ICSC
- CPAP side effects

CPAP side effects

- Dry eye and irritation secondary to air leakage around mask
- Increased incidence of bacterial conjunctivitis: probably related to above
  - Possible increased IOP during use: up to 5-8 points: ? If on glaucoma therapy

Recent study

- Study of 31 new CPAP users and 20 non-CPAP users
- Showed no increase in IOP with CPAP use
- Small sample size
- Not evaluated long term (new to CPAP use)
- Take home message: unclear if CPAP use increases IOP or not, as studies conflict

Floppy Eyelid Syndrome

- First described in 1981 by Culberston and Ostler
- Less than 5% of people with OSA have FES.............but essentially 100% of people with FES have OSA
- Most commonly overweight men
- Eyelids are very loose and rubbery
- Evert easily with minimal pressure
- Associated with keratoconus: Rubbing vs. elastic issue
- Moderate and severe OSA patients have a much higher rate of substantial Conjunctivochalasis

Floppy Eyelid Syndrome

- Lash ptosis very common
- Typically improves with control of OSA
- Relationship unclear, but may be due to changes in MMP leading to increased elasticity of tissue
- Problem comes when lids contact the pillow during sleep and evert or open

UNDERDIAGNOSED
Symptoms of F.E.S.
Dry, gritty, irritated eye or eyes upon awakening that get better as the day goes on
If patient always sleeps on one side, only that eye is affected
Punctate Keratitis
Conjunctivitis
Mucous discharge
Can then get Mucous Fishing Syndrome

Treatment of F.E.S.
Patient education
Weight loss and management of OSA
Night time lubricating ointment
Sleep with cylinder pillow ("dog bone" pillow)
Use firm sleep mask
Taping of lids (no one complies with this)
Surgical resection of tissue
Study Regarding FES and Glaucoma

Journal of Glaucoma 2014: 23; (1)

1) 75 patients with OSA but no FES
2) 52 patients with OSA and FES
3) 25 patients without OSA

% of patients with glaucoma of any type:

1) 5%
2) 23%
3) 0%

Papilledema

Some patients with OSA have increased ICP at night.
Lumbar tap opening pressure tends to be normal during waking hours.
Can lead to papilledema if severe enough.

Papilledema

Association unclear
Perhaps just having obesity as a common risk factor
But if so, why is ICP up only at night?
Also, treatment with CPAP decreases ICP
Consider especially in males with IIH

I.C.S.C. (Central Serous)

Recently linked in some patients to OSA
Unknown cause, perhaps related to increased epinephrine causing increased catecholamine levels
Keep possible link in mind

Glaucoma

OAG and NTG are both more common in patients with OSA.
Prevalence in various studies is highly variable.
Highest in literature are 27% of OSA patients in one study with OAG, 43% in another with NTG.

Most are much lower, but still well above the rate in the general population.

Especially common in NTG patients who progress despite very low IOP.

Glaucoma

Believed to be related to poor blood flow and decreased oxygen delivery to the optic nerve.
Especially important to consider with NTG.
Worth looking in to OSA with NTG patients who have symptoms.

Glaucoma
Study on glaucoma with OSA

Meta-analysis of 6 studies, 3 cohort and 3 case control
Considered multiple types of glaucoma
Overall............

Cohort studies showed a combined 1.43 fold risk of glaucoma with OSA
Case control studies showed a 2.46 fold risk
Overall a 72% increase in risk
Interestingly, no statistical increase in POAG. May be biased by inclusion of Chinese data with high rate of ACG

Plaquenil bonus material

Hydroxychloroquine
One of the most common reasons for routine ocular screening for adverse reaction
Used mostly for treatment of RA and Lupus, other emerging uses
About 150,000 people in the US

Chloroquine (Aralen)
Used as an antimalarial drug; very rarely for RA / Lupus
Much greater chance of ocular damage
 Rare to be on long term therapy

Plaquenil

If patients are on 200mg / day ocular problems are very rare
At 400mg / day for extended periods of time the risk is much greater
Ocular damage and symptoms can progress after meds have been D/C
Damage can be irreversible

NTG

Could OSA possibly explain Drance Hemorrhages?
How about the propensity for paracentral VF defects?

Plaquenil

Dose is 200mg or 400mg daily.
400mg common
Prescribed in 200 mg tablets
Occasionally see 300 mg per day used (cut pills in half)

Increased risks of ocular damage include....
daily dose over 5.0 mg/kg/day using strictly actual weight (old standard for many years was 6.5 mg/kg/day using ideal body weight; may still be best for short, obese patients)
Renal dysfunction
Other maculopathy
Tamoxifen use concurrently (5 X risk)

Plaquenil

Affects the photoreceptors and then the RPE
Stores in Melanotic tissue, the liver, and the kidney
Excreted mostly by the kidney
Damage begins in a ring around the center of the fovea: often begins inferior-temporally first thus affecting the VF superior nasal to fixation first
**Chance for retinal toxicity**

At doses below the 5.0 mg / kg / day threshold......

Marmor and Melles 2014: study of 2361 patients with use over 5 years: 177 with toxicity (7.5%); all doses included

- < 1% risk at 5 years
- < 2% risk at 10 years
- 20% risk at 20 years

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**Ocular side effects of Plaquenil**

- Bulls eye pigmentary maculopathy: late!
- Visual field loss
- Decreased vision and contrast sensitivity
- Color vision changes
- Vortex keratopathy (rare...more common with chloroquine)

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**Plaquenil management**

- Testing should include......
  - Baseline exam with fundus evaluation within one year of beginning medications
  - Management guidelines updated June 2016
- Looking for pre-existing pathology
- Supplementary diagnostic tests not needed at baseline visit

- Then after five years of use......
  - Yearly exams with 10-2 VF (white on white) and SD-OCT
  - Also can consider FAF and multifocal ERG as extra testing
  - See more frequently and before five years if extensive risk factors present or dose above threshold

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**VF defects with Plaquenil**

- HVF 10-2 white on white
- Use pattern deviation plot
- Look for paracentral ring scotoma or partial ring scotoma in area 2-6 degrees from center
- Take any defect, even modest defects of 4-8 DB, seriously

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**Courtesy Dr. Diana Shechtman**
Plaquenil management

Multifocal ERG (very sensitive, but extremely variable: should not be used alone),
SD-OCT (Flying Saucer sign), FAF.
Report to rheumatologist
Assess for dose toxicity at every visit
We have the ability to detect toxicity before vision loss occurs and before fundus changes are visible.

Chen et al. Clinical Ophthalmology 2010:4 p. 1151

Plaquenil management
Study in Ophthalmology (January 2014 on-line) showed... Out of 150 individuals showing clear toxicity after cumulative dose of over 1000g......
90% showed defects on both 10-2 VF and OCT
10% showed VF defect, but no OCT defect. Zero with OCT but no VF defect.

Showed that the opposite can occur: 17 eyes found that had early OCT defects (attenuated PIL line or loss of parafoveal interdigitation zone) but no VF loss.

Late progression
Marmor and Hu JAMA online June 2014
11 patients with toxicity
Followed for three years after D/C Plaquenil
Categorized as mild / moderate / severe toxicity
Mild / moderate showed no progression after D/C
Severe progressed for up to three years
A second, 2018 study of 13 patients (some the same as above, some different) showed that some severe patients with RPE damage progressed for over 20 years!

Late progression
Basically no progression of VA or VF loss
Significant progression in severe cases of SD-OCT and FAF damage
May be related to eventual death of already critically damaged RPE cells and foveal cones
Plaquenil found in blood in low amounts one year after D/C

Bull’s Eye Maculopathy
Bull’s Eye Maculopathy

5 cases of Bull’s Eye Maculopathy reported with Sertraline (Zoloft)
An SSI used for depression
Very rare, but very significant

One case involved a 14 year old whose vision dropped to 20/200 in each eye after one year of use. Did not recover or improve after three years off of the drug.

Chloroquine maculopathy

Critical caveat
In Asian patients, damage tends to be paramacular and can extend out to the arcades
More diffuse maculopathy instead of a bullseye pattern

Must perform 24-2 or 30-2 VF instead of a 10-2 because damage tends to be further out
SD-OCT scans need to be performed outside of the fovea too
FAF a good choice

Chloroquine maculopathy & FAF
Chloroquine OCT

Chloroquine OCT En-face

Plaquinil toxicity

Plaquinil toxicity OCT

Plaquinil Toxicity FAF

Plaquinil toxicity En Face OS