Obstructive Sleep Apnea and Diabetes: pathophysiology, diagnosis and treatment

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Objectives

Provide overview of obstructive sleep apnea (OSA)

- Epidemiology
- Definitions
- Pathophysiology
- Clinical Evaluation
- Diagnosis
- Treatment and follow up management
What is the prevalence of sleep disordered breathing (SDB)?

• Impacts about 20 million American adults
• Moderate to Severe OSA\textsuperscript{1}
  • Age 30-70
    • 10-17% Men
    • 3-9% Women
• 85-90% are undiagnosed and untreated

Epidemiological link between OSA and type 2 diabetes

• OSA is an independent risk factor for the development of type 2 diabetes
  • 15-30 % of patients with OSA have type 2 diabetes

• Sleep Health Heart Study
  • Mild and Moderate to Severe OSA was associated with impaired glucose tolerance compared to subjects without OSA
  • Severity of nocturnal hypoxia independently associated with glucose intolerance

Prevalence of OSA in participants with type 2 diabetes

• The Sleep Action for Health in Diabetes (AHEAD) study
• 306 participants had sleep testing
  • 86.6% had an apnea hypopnea index (AHI) indicative of OSA
  • Mean AHI was 20.5+/-16.8/hr
  • 30.5% had moderate OSA
  • 22.6% had severe OSA

What is Obstructive Sleep Apnea?

- OSA (Obstructive Sleep Apnea) occurs when the upper airway repeatedly collapses during sleep, causing cessation of breathing (apnea) or inadequate breathing (hypopnea) and sleep fragmentation.
Hypopnea
Obstructive Apnea. A complete blockage of the airway despite efforts to breath. Notice the effort gradually increasing ending in airway opening.
OSA pathophysiology: intermittent hypoxia and sleep fragmentation

Wakefulness

Sleep

- **Airway Patency Compensation**
- **Decreased Compensation**
- **Airway Collapse**
- **Hyperventilation**
  - $O_2$ & $CO_2$
- **Increased Effort to Breathe**
- **Arousal Sleep**

OSA pathophysiology: intermittent hypoxia and sleep fragmentation
OSA pathophysiology: sympathetic activation

Wakefulness

Sleep

Airway Patency Compensation

Decreased Compensation

Airway Collapse

Arousal & Hyperventilation

\( O_2 \) & \( \text{CO}_2 \)

Sympathetic Activation

Increased RR
Increased mental activity
Increased BP
Increased HR
Increased release of glucose

\( O_2 \) & \( \text{CO}_2 \)
Obstructive Sleep Apnea
- Hypoxemia
- Reoxygenation
- Hypercapnia
- Intrathoracic Pressure Changes
- Arousals

**Intermediary Mechanisms**
- Sympathetic Activation
  - Vasoconstriction
- Increased Catecholamines
- Tachycardia
- Impaired Cardiovascular Variability
- Endothelial Dysfunction
- Vascular Oxidative Stress
- Inflammation
- Increased Coagulation
- Metabolic Dysregulation
  - Leptin Resistance
  - Obesity
  - Insulin Resistance

**Risk of Cardiovascular Disease**
- Hypertension
- Congestive Heart Failure
  - Systolic Dysfunction
  - Diastolic Dysfunction
- Cardiac Arrhythmia
  - Bradycardia
  - A-V Block
  - Atrial Fibrillation
- Cardiac Ischemia
  - Coronary Artery Disease
  - Myocardial Infarction
  - Nocturnal ST-Segment Depression
  - Nocturnal Angina
- Cerebrovascular Disease
Central Adiposity → Sleep-disordered Breathing

- Intermittent Hypoxemia
- Sleep Fragmentation

Sympathetic System → Pituitary

- HPA Axis
- Somatotropic Axis

Leptin → TNF-α → IL-6 → Catecholamines

Glucose Intolerance → Insulin Resistance → Type-2 Diabetes Mellitus

Cortisol

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Potential health consequences if untreated

**Short-term**
- Automotive accidents
- Excessive sleepiness
- Decreased quality of life
- Neurocognitive and performance deficits

**Long term**
- Hypertension
  - 30 to 50% of patients with OSA have hypertension\(^1\)
  - Patients with untreated OSA may be resistant to their medication\(^2\)
- Heart Failure
  - 40 to 50% of patients with CHF have OSA\(^3\)
- Atrial fibrillation
  - Adjusted odd ratio associating A Fib and OSA is 2.19.\(^4\)
- Diabetes
  - 87% of obese Type II Diabetics have OSA\(^5\)

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1. Kraicze, et al., AJRCCM 2000
2. Logan, et al., J Hypertens 2001
• Recommendation from the International Diabetes Federation Taskforce:
  • All patients with type 2 diabetes should be screened for OSA
How can you use this information?

• What role do you play?
Type of patients to consider screening

• Complain of fatigue or unrefreshing sleep
• Hypertension
  • Newly identified hypertension
  • Resistant or refractory hypertension
• CHF with nocturnal angina or cardiovascular disease
• Bariatric patients
• Patients with large necks
  • 17 in for men, 16 in for women
• Patients with small jaws
• Patients with metabolic syndromes
  • (such as diabetes)
Additional signs/symptoms of OSA

- Recurrent nocturnal awakenings
- Un-refreshing sleep
- Daytime fatigue
- Impaired concentration/memory loss
- Mood/behavioral changes
- Morning headaches
- Loss of sexual interest
Risk factors for OSA

- Hypertension - refractory hypertension
  - increased healthcare utilization
- Ethnicity
- Family history OSA
- Body Mass Index (BMI) > 30
- Large neck circumference
  - Male > 17 in
  - Women > 16 in
  - Physical characteristics
  - crowded airway
  - facial characteristics
Case Presentation: History

• 44 year old male was referred for evaluation with the complaint of excessive daytime sleepiness (EDS)

• Symptoms
  • Snoring
  • Spouse witnessed apneas
  • Dry mouth in AM
  • Morning headaches daily

• 3 car accidents over the last year
Case history continued...

• Past Medical History: hypertension
• Past Surgical History: none
• Social History: consumes 6 caffeinated beverages/day, no alcohol or tobacco
• Medications: hydrochlorothiazide, lisinopril, amlodipine
• ROS: Denies insomnia, restless leg, sleep paralysis or any other concerning sleep symptoms
Case presentation: Physical Examination

- Neck circumference of 18 inches
- HEENT: Mallampati Class I
Mallampati Airway Classification (I-IV Scale)

Nuckton TJ; Glidden DV; Browner WS et al. Physical examination: Mallampati score as an independent predictor of obstructive sleep apnea. SLEEP 2006;29(7):903-90
Methods for OSA screening

• Epworth Sleepiness Scale

• Berlin Questionnaire

• STOP-Bang
## Epworth Sleepiness Scale

<table>
<thead>
<tr>
<th>Activity</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sitting and reading</td>
<td>3</td>
</tr>
<tr>
<td>Watching TV</td>
<td>3</td>
</tr>
<tr>
<td>Sitting, inactive in a public place</td>
<td>2</td>
</tr>
<tr>
<td>As a passenger in a car for an hour without a break</td>
<td>3</td>
</tr>
<tr>
<td>Lying down to rest in the afternoon when circumstances permit</td>
<td>2</td>
</tr>
<tr>
<td>Sitting and talking to someone</td>
<td>0</td>
</tr>
<tr>
<td>Sitting quietly after a lunch without alcohol</td>
<td>2</td>
</tr>
<tr>
<td>In a car, while stopped for a few minutes in traffic</td>
<td>3</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>18/24</td>
</tr>
</tbody>
</table>

0 = would *never* doze  
1 = *slight* chance of dozing  
2 = *moderate* chance of dozing  
3 = *high* chance of dozing

STOP-Bang Scoring Model

1. Snoring
   Do you snore loudly (louder than talking or loud enough to be heard through closed doors)?
   Yes  No
2. Tired
   Do you often feel tired, fatigued, or sleepy during daytime?
   Yes  No
3. Observed
   Has anyone observed you stop breathing during your sleep?
   Yes  No
4. Blood pressure
   Do you have or are you being treated for high blood pressure?
   Yes  No
5. BMI
   BMI more than 35 kg/m^2?
   Yes  No
6. Age
   Age over 50 yr old?
   Yes  No
7. Neck circumference
   Neck circumference greater than 40 cm?
   Yes  No
8. Gender
   Gender male?
   Yes  No

*High risk of OSA*: answering yes to three or more items

*Low risk of OSA*: answering yes to less than three items
The Berlin Questionnaire

• Simple, self-administered patient questionnaire
• Uses ten questions to assess:
  • Presence & frequency of snoring behavior
  • Wake-time sleepiness or fatigue
  • History of hypertension and/or obesity
• Persistent or frequent symptoms in two of three categories indicates a high likelihood of OSA
Diagnosis of sleep apnea

- History and physical exam
- Screening tools
- Diagnosed by having a polysomnogram or sleep study performed during the patient’s normal sleep time
# Levels of Diagnostic Sleep Equipment

<table>
<thead>
<tr>
<th>Level I</th>
<th>Level II</th>
<th>Level III</th>
<th>Level IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard polysomnography</td>
<td>Comprehensive portable polysomnography</td>
<td>Modified portable sleep apnea testing</td>
<td>Continuous single- or dual-bioparameter recording</td>
</tr>
<tr>
<td><strong>Parameters</strong></td>
<td><strong>Parameters</strong></td>
<td><strong>Parameters</strong></td>
<td><strong>Parameters</strong></td>
</tr>
<tr>
<td>Minimum of seven, including EEG (C4-A1 or C3-A2), EOG, chin EMG, ECG, airflow, respiratory effort, oxygen saturation</td>
<td>Minimum of seven, including EEG (C4-A1 or C3-A2), EOG, chin EMG, ECG or heart rate, airflow, respiratory effort, oxygen saturation</td>
<td>Minimum of four, including ventilation (at least two channels of respiratory movement, or respiratory movement and airflow), heart rate or ECG, oxygen saturation</td>
<td>Minimum of one</td>
</tr>
<tr>
<td><strong>Body position</strong></td>
<td><strong>Body position</strong></td>
<td><strong>Body position</strong></td>
<td><strong>Body position</strong></td>
</tr>
<tr>
<td>Documented or objectively measured</td>
<td>May be objectively measured</td>
<td>May be objectively measured</td>
<td>Not measured</td>
</tr>
<tr>
<td><strong>Leg movement</strong></td>
<td><strong>Leg movement</strong></td>
<td><strong>Leg movement</strong></td>
<td><strong>Leg movement</strong></td>
</tr>
<tr>
<td>EMG or motion sensor desirable but optional</td>
<td>EMG or motion sensor desirable but optional</td>
<td>May be recorded</td>
<td>Not recorded</td>
</tr>
<tr>
<td><strong>Personnel</strong></td>
<td><strong>Personnel</strong></td>
<td><strong>Personnel</strong></td>
<td><strong>Personnel</strong></td>
</tr>
<tr>
<td>In constant attendance</td>
<td>Not in attendance</td>
<td>Not in attendance</td>
<td>Not in attendance</td>
</tr>
<tr>
<td><strong>Interventions</strong></td>
<td><strong>Interventions</strong></td>
<td><strong>Interventions</strong></td>
<td><strong>Interventions</strong></td>
</tr>
<tr>
<td>Possible</td>
<td>Not possible</td>
<td>Not possible</td>
<td>Not possible</td>
</tr>
</tbody>
</table>

Abbreviations used: EEG, electroencephalogram; EOG, electrooculogram; EMG, electromyogram; ECG, electrocardiogram.

Alright, sleep tight, all night ~ don't let the bed bugs bite!
Technologists monitor your patients for 6-8 hours
In-Lab Polysomnography
Portable Monitoring
AASM Clinical Guidelines: Portable Monitoring

- Performed only with a comprehensive sleep evaluation
- Alternative for the diagnosis of OSA in patients with high pretest probability for moderate/severe OSA
- May be indicated in patients whom in-lab PSG is not possible
  - Immobility
  - Safety
- No co-morbid conditions (pulmonary disease, neuromuscular disease or CHF)
- Not appropriate for pts suspected of having other sleep disorders (PLMS, insomnia, parasomnias, etc.)
Treatment of sleep disordered breathing

- Positive airway pressure
  - Continuous positive airway pressure
  - Bi-level positive airway pressure
- Oral appliances
- Other
  - Weight loss
  - Surgery
Positive Airway Pressure (PAP) a historical perspective

Continuous positive airway pressure (CPAP) for the treatment of OSA was first described by Colin Sullivan and coworkers in the 1980’s.
OSA therapy

- Of those patients being treated for OSA, 70 - 80% utilize CPAP therapy with a nasal mask\textsuperscript{1}
- CPAP provides positive pressure to provide a pneumatic splint for the patient’s airway

\textsuperscript{1} Frost & Sullivan, Sleep Apnea Models, 2001
Goals of treating OSA with PAP

Short term

• Maintain open airway
• Improve quality of sleep
• Alleviate daytime symptoms
  • Sleepiness
  • Moodiness/Impaired concentration/Memory loss
  • Morning headache

Long term

• Reduce mortality and morbidity
  • Decrease cardiovascular consequences
  • Reduce sleepiness
• Improve quality of life

Indications for PAP treatment

- Center for Medicare Services
  - OSA dx by >2hrs PSG in a sleep lab
  - AHI $\geq$ 15/hr
  - AHI $\geq$ 5/hr with symptoms (daytime sleepiness, impaired cognition, mood disorders) or co-morbid conditions (hypertension, stroke, coronary artery disease)
CPAP therapy and diabetes

- Effective treatment of SDB led to improved glycemic control in subjects with Type II diabetes*
  - In subjects who used CPAP > 4 hrs/day, ↓ in HbA1c significantly correlated with days of CPAP use

*Mean CPAP treatment period of 83 days

Non CPAP treatment of OSA

• Weight loss
  • 10% loss can improve AHI

• Dental appliances
  • Mild to moderate OSA
  • Side effects: increased salivation, TMJ pain, myofacial pain, dry mouth, gum irritation
  • Contraindications: edentulous or <6 healthy teeth in each arc
Long-term Management and PAP adherence
CPAP therapy adherence

• How is OSA treatment adherence defined?
  • > 4 hours of use, >70% of time (Kribbs\textsuperscript{1})
  • Studies show patient adherence to therapy is not ideal but similar to maintenance medications\textsuperscript{2}
  • Kribbs found that 54% could be inconsistent users\textsuperscript{1}

1 Kribbs, et al., Objective Measurement of Patterns of Nasal CPAP Use by Patients with OSA. American Review of Respiratory Disease 1997:147 No. 4
Medicare’s definition of compliance

Adherence to therapy is defined as use of PAP ≥ 4 hours per night on
70% of nights during a consecutive thirty (30) day period anytime during
the first three (3) months of initial usage.*

* Reference LCD for Positive Airway Pressure (PAP) Devices for the Treatment of Obstructive Sleep Apnea (L11528)
What do we know about CPAP adherence?

• In a landmark study, 54% of patients were found to be inconsistent users of CPAP\(^2\). The effectiveness of CPAP is in question when used inconsistently.

• Skipping CPAP for two or more nights within the first week of treatment signals potential non-adherence and emphasizes the need for close follow-up during this period of time\(^1\)

• The first week to month of home therapy appears to be the most critical phase for intervention and securing long-term compliance.\(^2\)

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Common problems with CPAP therapy

Adapted from Rosenthal, L.; Sleep, 2005
PAP settings to consider

- Acceptable $\text{EPAP}_{\text{min}}$ setting on APAP
- Comfort settings on exhalation
  - Provide relief during exhalation phase to allow for improved comfort to CPAP therapy
- When to use comfort settings:
  - Initial set up
  - Pressure intolerance
  - Difficulty with acclimation to PAP therapy

Aloia, et. al. Treatment adherence and outcomes in flexible vs. standard CPAP therapy, Chest, June 2005
PAP settings to consider continued...

- **Ramp**
  - Allows for patient to fall asleep at a lower pressure and acclimate to pressure over time
  - Can be adjusted based on pressure drop and length of time until patient is back at prescribed PAP pressure while falling asleep
Other tools

• Finding the optimal patient interface type, size and fitting
• Nasal
  • A common starting mask for OSA patients
• Full
  • Good for mouth breathers
• Pillows/prongs
  • Claustrophobia
  • Side sleepers
• Chinstrap may be used for mouth leak with nasal interfaces
• MANAGE LEAKS
CPAP non-adherence and education

• Hindrance to CPAP compliance
  • Poor patient education
  • Poor understanding of the disease management process

• Supportive interventions enhance the use of CPAP therapy by 0.59 hours/night\textsuperscript{1}

\textsuperscript{1} Donepudi et al., Touch Point Care and Advanced Monitoring Technologies Improves Compliance Rate of CPAP Usage, Abstract 1300, APSS 2012.
Consequences of non-adherence to CPAP therapy for the OSA patient

Summary

• OSA afflicts at least 25 million adults in the U.S., according to the National Healthy Sleep Awareness Project.

• OSA is a chronic disease that increases the risk of high blood pressure, heart disease, stroke and type 2 diabetes.

• Diagnosis and screening procedures used to identify OSA – Epworth, Berlin, STOP bang

• Various treatment options of OSA- PAP, oral appliances, weight loss

• Long term management--patient education and support have been shown to increase CPAP adherence
Questions?