Review and Updates in Clinical Sleep Medicine

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Objectives

- **Sleep-related Breathing disorders**
  - Obstructive Sleep Apnea
  - Central Sleep Apnea

- **Sleep-related Movement Disorders**
  - RLS
  - PLMD

- **REM-related Sleep Disorders**
  - Narcolepsy
  - REM Behavior Sleep Disorder
Sleep-related Breathing Disorders:
Obstructive Sleep Apnea
Central Sleep Apnea

Apnea = complete cessation of airflow >10s
Hypopnea = >30% reduction of airflow for >10s with >4% drop in saturation
AHI = Apnea-Hypopnea Index
- Normal 0-5
- Mild 5-15
- Moderate 15-30
- Severe >30
RDI = total respiratory events per hour
RERA = respiratory event related arousal
- Esophageal manometry showing crescendo or increased inspiratory effort followed by arousal
- Snore-related arousal

Hypnogram
Prevalence

- AHI > 5:
  - 15% middle-aged men
  - 9% middle-aged women

- OSA Syndrome
  - 4-9% middle-aged men
  - 2-4% middle-aged women

Pathophysiology

Anatomical predisposition AND Functional impairment

Physical Exam
Risk Factors

- Obesity (BMI > 30)
- Male
- Age (middle-age, post-menopausal)
- Ethnicity (Asian)
- Neck Size (> 17 in men, >15 in women)
- Abnormal craniofacial morphology
- Down’s Syndrome
- Parkinson’s Disease
- Hypothyroidism
- Excessive GH
- Post-CVA

Symptoms

- Excessive Daytime Somnolence
- Headaches
- Lack of concentration
- General malaise
- Performance impairment
- Depressed mood
- Irritability
- Insomnia
- Hyperactivity

Comorbidities

- Hypertension
- Heart failure
- Arrhythmias
- Stroke
- Coronary Artery Disease
- Pulmonary Hypertension
- Hypercoagulopathy
- Depression
- Obesity
- Diabetes
- Preeclampsia
- GERD
- Seizures
- Parasomnias
- Headaches

Wisconsin Sleep Cohort Study

**Table 3. Adjusted Odds Ratios for Hypersomnia at a Follow-up Sleep Study, According to the Apnea-Hypopnea Index at Baseline.**

<table>
<thead>
<tr>
<th>Category</th>
<th>Odds Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>0.5-1.9 events/hr</td>
<td>1.66 (1.33-2.08)</td>
<td>1.66 (1.33-2.08)</td>
</tr>
<tr>
<td>2.0-4.9 events/hr</td>
<td>2.74 (1.82-4.12)</td>
<td>2.74 (1.82-4.12)</td>
</tr>
<tr>
<td>&gt;5.0 events/hr</td>
<td>4.54 (2.44-8.36)</td>
<td>4.54 (2.44-8.36)</td>
</tr>
</tbody>
</table>

JNC Recommendations

- **JNC VI (1997)**
  - OSA should be ruled out in refractory HTN

- **JNC VII (2003)**
  - OSA should be first on the list of identifiable causes of HTN

**Table 4. Identifiable causes of hypertension**

- **Sleep apnea**
- Drug-induced or related causes (see table 9)
- Chronic kidney disease
- Primary aldosteronism
- Renovascular disease
- Chronic steroid therapy and Cushing’s syndrome
- Pheochromocytoma
- Coarctation of the aorta
- Thyroid or parathyroid disease
  (adapted from JNC VII)

Diastolic Dysfunction

- 55% with diastolic dysfunction have SDB, mostly OSA
- LVH found in 88% of severe OSA
- Suspect OSA if have CHF due to diastolic dysfunction, or LVH on EKG or ECHO without evidence of valve disease or HTN
- Mechanisms include hypertension, trophic effects of endothelin and catecholamines which are elevated in OSA

Arrhythmias

- Sinus bradycardia and AVB are most common as a result of diving reflex
  - Bradycardia related to duration of apnea and degree of desaturation
- Atrial fibrillation, PAC, PVC next most common
  - Occurs during termination of apneic episode and during REM
- Proportion of patients with OSA was significantly higher in the AF group than in the general cardiology group (49% versus 32%, P=0.0004)

- Adjusted OR for the association between AF and OSA was 2.19 (95% CI 1.40 to 3.42, P=0.0006)

- 12 months after successful cardioversion for AFib, 84% untreated OSA, 42% treated OSA, 53% non-OSA reconverted

- Unresolved if OSA an independent RF for arrhythmias

Circulation 2003;107:2589-94

- **CPAP**
  - Surgery
  - Oral appliance
  - Provent
  - Weight loss
  - Positional therapy
  - Avoid alcohol and sedating medications
  - Drugs

**Treatments**

- Most efficacious
- Poor compliance (40-60%)
- CMS reimbursement guidelines
  - AHI > 15/hr, or 5-15/hr with clinical sequelae

**CPAP**

- Close follow-up and education
- Sleep during titration
- Heated humidification
- APAP or Bilevel
- Flex pressures
- Ramp feature
- Hypnotics, anxiolytics
- Exposure to CPAP before initiation of therapy
- Treatment of nasal resistance
- Patient-centered mask and device selection
- Bed partner involvement and support

**Improving Compliance**
Definition of success in surgical literature is >50% reduction of AHI and/or an AHI <20

- **UPPP**: 40–50% for mild-mod OSA, although efficacy appears to decrease over time
- **GA**: 35–60% depending on the severity
- **TNA**: 75–100% in children, with complete cure in 60–80% of cases
- **MMA** ~90%, with an average improvement in AHI > 85%

**Hypoglossus Nerve Stimulator**

- SSRI paroxetine increases GG activity and attenuates reflex GG muscle inhibition by PAP
- Fluoxetine and paroxetine improves AHI in moderate OSA patients
- Paroxetine causes no improvement in AHI with severe OSA (AHI>60)

Potential Drug Therapies

- Mirtazapine
- Acetazolamide
- Carbon Dioxide
- Medroxyprogesterone
- Aminophylline
- Theophylline
- Physostigmine
- Protriptyline
- Thyroxine
- Mibefradil
- Cilazapril
- Buspirone
- Doxapram
- Ondansetron
- Sabeluzole
- Nicotine
- Clonidine

Central Sleep Apnea

- Puhan et al. Didgeridoo playing as alternative treatment for OSAS: Randomized Control Trial. BMJ 2006;332(7536):266
- Rarer type of SBD
- 90% Idiopathic
- Cheyne Stokes Breathing, High-Altitude Periodic Breathing, Drugs, Congenital
- High Loop Gain

Central Sleep Apnea

Cheyne Stokes Breathing

- RF for CSA in HF is male, hypocapnia, afib, >60 yrs
- Present in 25-40% of patients with heart failure
- CSA is associated with greater mortality in HF

Central Sleep Apnea and Heart Failure

Canadian Continuous Positive Airway Pressure for Patients with Central Sleep Apnea and Heart Failure Study
- 258 patients with heart failure (mean EF 24.5%) and CSA (AHI 40)
- Randomized to CPAP or no CPAP for 2 years

CANPAP study

Circulation. 2007;115:3173-3180
- Improvement in AHI for CPAP group
- Decrease in norepinephrine level (p=0.009)
- Improvement in EF (2.2% vs. 0.4 %, p=0.02)
- No difference in number of hospitalizations, quality of life, ANP levels
- Follow up study showed that in patients whom the AHI decreased to < 15, there was significant improvement in transplant-free survival (hazard ratio 0.37 [0.14 to 0.97], P=0.043)

**CANPAP study**

- Optimize treatment of underlying condition
- CPAP
- Bilevel S/T
- ASV (Servo-ventilation)

**Treatment**

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**Sleep-related Movement Disorders:**
- Restless Leg Syndrome
- Periodic Limb Movement Disorder
Restless Leg Syndrome

- Prevalence: 7-10% (3% severe), 15% pregnant women
- Clinical Diagnosis - 4 criteria:
  1. An urge to move, usually due to uncomfortable sensations (described as creeping, crawling, aching), primarily in the legs
  2. Urge to move partially/totally relieved by movements (walking/stretching)
  3. Worsening of symptoms by relaxation; improved if move legs
  4. Day to day variability but generally worse in evening and early in the night

Secondary Restless Leg Syndrome

- Iron deficiency
  - If ferritin < 50, replace iron to ferritin > 100
  - RCT of oral iron X 12 wks reduced RLS symptoms (Wang J; Sleep Med 2009)
- Antidepressants
- Antihistamines
- Alcohol
- Pregnancy
- Chronic kidney disease
- Diabetes
- BZD withdrawal
- Thyroid disease
- Varicose veins

Periodic Leg Movement Disorder

- Polysomnograph diagnosis
- Occurs during sleep
- Characteristic EMG discharges every 20-40 sec associated with arousals
- PLMI > 15
- PLMs seen in ~80% of patients with RLS and are supportive features of a diagnosis of RLS
- Non-pharmacologic
  - Hot showers, compresses, stretching, massages

- Pharmacologic
  - Dopamine agonists:
    - Ropinirole (Requip) – 2005
    - Pramipexole (Mirapex) – 2006
    - Rotigotine (Neupro) – 2007
  - Carbidopa/Levidopa
  - Benzodiazepines
  - Anti-convulsants:
    - Carbamazapine
    - Gabapentin
  - Opioids

**Outcomes**
- Insomnia, daytime sleepiness
- Migraines
- Hypertension
- Heart Disease, Stroke

**REM-related Sleep Disorders:**
- **Narcolepsy**
- **REM Behavioral Disorder**

**Narcolepsy**
- Prevalence 1:2000 (0.05%)
- HLA DQB1*0602
- Hypocretin or orexin deficiency
- Autoimmune Disorder

- First symptoms usually EDS or sleep attacks, appears in teens
- Followed months to years later by (1) cataplexy (pathononmonic), (2) sleep paralysis, (3) hypnogogic/hypnic hallucinations
- PSG + MSLT
• PSG to rule out other sleep disorders
• MSLT:
  ◦ Patient must keep a regular sleep schedule >2 wks prior
  ◦ Adequate sleep hours
  ◦ Off REM suppressing medications (e.g. SSRIs), sedating medications, stimulants for >2 wks prior

Narcolepsy

• EDS:
  ◦ Methylphenidate (Ritalin)
  ◦ Amphetamines (Adderall, Dexedrine)
  ◦ Modafinil (Provigil, Nuvigil)
  ◦ Atomoxetine (Strattera)
  ◦ Scheduled naps!

• Cataplexy:
  ◦ SNRI
  ◦ SSRI
  ◦ Gamma hydroxybutyrate (Xyrem)

REM Behavior Disorder

<table>
<thead>
<tr>
<th>RBD</th>
<th>Somnambulism (Sleepwalking)</th>
</tr>
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<tbody>
<tr>
<td>Features</td>
<td>&quot;Acting out dreams&quot; Eyes closed</td>
</tr>
<tr>
<td>Sleep stage</td>
<td>REM</td>
</tr>
<tr>
<td>PSG</td>
<td>EMG tone excess during REM sleep (i.e lack of REM atonia)</td>
</tr>
<tr>
<td>Demographics</td>
<td>Men, &gt;50 yrs Neurological disorders</td>
</tr>
<tr>
<td>Prevalence</td>
<td>0.5% adults 67% PD 90% MSA</td>
</tr>
<tr>
<td>Course</td>
<td>Progressive</td>
</tr>
<tr>
<td>Treatment</td>
<td>Clonazepam</td>
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Summary

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