Health Related Consequences of Obstructive Sleep Apnea and Response to Therapy

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Consequences of OSA

• Subjective complaints: snoring, sleepiness
• Neuropsychological sequelae
• Metabolic Derangements
• Hypertension
• Heart and Vascular Disease
Neurobehavioral Effects

- Sleepiness/tendency to fall asleep
  - Epworth Sleepiness Scale is commonly used subjective test of sleepiness
  - The MSLT is a polysomnographic test of sleep tendency requiring subjects to try to fall asleep during daytime nap opportunities lasting 20 min or less. The latency from lights out to sleep onset is the principal outcome measure. Patients with severe OSA often have mean sleep onset latencies in the pathological range of 5 minutes or less, some 2 SD below normal mean values of 12.
  - MWT and OSLER testing also delineate degree of sleepiness in pts with OSA
Neurobehavioral Effects

- Sizable effect of OSA on the ability to sustain attention over time, particularly on the quality of the performance rather than simple reaction time.
- Moderate to severe OSA negatively impacts memory and executive performance—although presence and degree of deficit in these categories is controversial.
- QOL studies indicate that pts with OSA have significantly impaired QOL and social functioning and a high prevalence of minor psychiatric morbidity.
Neurobehavioral Effects and Treatment

- Improvements in both subjective and objective tests of sleepiness are seen with CPAP therapy for OSA. These improvements are moderate to large. Subjective scores improve to a larger degree than objective scores.

- Evaluation of attention-based cognitive outcomes, there is a much more modest improvement of functioning with CPAP.

- QOL: the large impairments in sleepiness and energy related QOL scores show substantial improvement with CPAP—those with the most severe OSA reap the most benefit.
Metabolic Effects

- **Insulin Resistance**: hyperglycemia resulting from both an impaired insulin secretory response to glucose and decreased insulin effectiveness in stimulating glucose uptake by skeletal muscle and in restraining hepatic glucose production.

- **Metabolic Syndrome**: hyperinsulinemia, glucose intolerance, dyslipidemia, central obesity, and hypertension; all risk factors for vascular disease.
OSA and Impaired Glucose Metabolism

- **Meslier et al 2003**
  - 595 male patients referred for polysomnography underwent a 2 hour oral glucose tolerance test.
  - 494 pts had OSAS (AHI > 10)
  - Fasting and postload blood glucose increased with severity of sleep apnea
  - Insulin sensitivity decreased with increasing severity of sleep apnea
  - BMI, age and AHI are all independent effect on blood glucose and insulin sensitivity
    - **Ip et al 2002**
      - 185 pts with OSAS (AHI>5)
      - Insulin resistance increased with age obesity (main determinant)
      - Independent determinants of OSA were AHI and min 02 sat

- **Punjabi et al 2003 [Review]**
  - Habitual snoring is associated with abnormal fasting glucose and insulin values independent of age and BMI
  - Prospective data from two separate studies indicate that habitual snoring is associated with more than a 2-fold risk of developing DM type II over a ten year period independent of BMI and other confounders
  - Several studies have suggested that the minimum oxygen saturation and AHI are predictive of glucose intolerance and insulin resistance independent of BMI, age and waist to hip ratio
Mechanism of Insulin Resistance

- Altered adrenergic function
- Direct effects of hypoxemia on glucose regulation
- Release of proinflammatory cytokines that affect metabolism
Effect of CPAP

- **Babu et al 2005**
  - 25 pts with DM type II, obesity (mean BMI 42.7), and OSA (mean AHI 56) were evaluated before and after a 90 day trial of CPAP
  - There were significant reductions in postprandial glucose values
  - Concluded that OSA is pathophysiologically related to impaired glucose homeostasis and that CPAP is an important therapy for pts with DM type II and OSA

- **Harsch et al 2003**
  - Forty patients with AHI>20 were evaluated for insulin sensitivity before, 2 d after and 3 mos after treatment with CPAP. Insulin sensitivity significantly increased after two days and remained stable after three months of treatment.
  - Patients with BMI < 30 had a much greater improvement in insulin sensitivity.
Hypertension

- **Wisconsin Sleep Cohort Study**
  - Increased risk for development of HTN in pts with OSA over a 4 to 8 year follow up period
  - Severity of OSA increased risk for development of HTN independent of baseline HTN status, age, gender, BMI, alcohol and cigarette use

- **Sleep Heart Health Study**
  - Large cross-sectional study (6132 participants)
  - Elevated risk for HTN found in subjects with SDB after adjusting for demographics, BMI, alcohol consumption and smoking
  - Association between SDB and HTN was seen regardless of age, gender, ethnicity, BMI
Mechanism

- Individual episodes of sleep apnea cause acute surges in HR and BP at apnea termination driven by HYPOXIA
- Epidemiologic evidence and physiologic studies in humans and animals support the idea that chronic exposure to repeated apneas may lead to a sustained diurnal HTN via increased SYMPATHETIC TONE and activation of the RENIN-ANGIOTENSIN SYSTEM
Treatment

- Treatment of OSAS does appear to lower blood pressure although the literature is inconsistent
- A recent randomized, double-blind, placebo-controlled study compared the effects of 2 weeks of CPAP versus sham-CPAP versus supplemental nocturnal oxygen on 24-hour ambulatory blood pressure in 46 patients with moderate-severe OSA
  - CPAP therapy resulted in a significant reduction in daytime mean arterial and diastolic blood pressure and nighttime systolic, mean, and diastolic blood pressure
  - Nocturnal supplemental oxygen therapy improved oxyhemoglobin saturation, it did not affect blood pressure.
Heart and Vascular Disease

- **Marin** et al published results of a 10-year observational study of:
  - 377 primary snorers
  - 403 patients with untreated mild to moderate OSA
  - 235 patients with severe OSA who refused treatment
  - 372 patients with OSA treated with CPAP
  - 264 healthy patients

- The endpoints [myocardial infarction, stroke, or acute coronary insufficiency requiring invasive management, death of myocardial infarction or stroke] were 3 times as high in patients with untreated severe apnea as in the healthy control individuals.

- **Milleron** et al prospectively monitored 54 patients with both CAD (>=70% coronary artery stenosis) and OSA (AHI >=15), 25 of whom were treated with CPAP or upper airway surgery and 29 who declined treatment for OSA, for a median of 86.5 ± 39 months. The endpoint (cardiovascular death, acute coronary syndrome, hospitalization for heart failure, or need for coronary revascularization) was reached in only 24% of the treated patients compared with 58% of those who declined OSA treatment.
Abnormalities associated with OSA may be intermediary mechanisms that contribute to the initiation and progression of cardiac and vascular pathology

- Sympathetic activation
  - Vasocostriction
  - Tachycardia
  - Increased catecholamines
- Endothelial dysfunction
  - Increased levels of endothelin may contribute to sustained vasoconstriction
- Vascular oxidative stress
  - Production of free radicals and vascular wall ischemia-reperfusion injury
- Inflammation
  - Increased CRP
- Increased coagulation
- Metabolic dysregulation
  - Insulin resistance
Conclusions

- OSA is implicated in neuropsychological changes that affect QOL; these changes can be modified with treatment.
- OSA has been identified as an independent risk factor for HTN and insulin resistance; both of these outcomes appear to be modified by treatment.
- OSA is indirectly implicated in cardiac and vascular disease.
Questions

• Should wider OSA screening be done for patients with evidence of cardiovascular disease?

• What are the long term effects of OSA treatment in terms of cardiovascular morbidity and mortality?

• Which interventions for OSA yield the highest benefit for the patient at the lowest cost?
Quiz #1

• **Epworth scale**
  - A. Refers to an objective measure of daytime somnolence
  - B. Refers to a subjective measure of daytime somnolence
  - C. Is a scale used to measure cognitive dysfunction associated with OSA
Quiz #2

• Insulin resistance:
  – A. is related to obesity
  – B. is related to OSA
  – C. is related to obesity and, to a lesser extent, OSA
  – D. is related to OSA and, to a lesser extent, obesity
Quiz #3

- Insulin sensitivity
  - A. Has been shown to markedly improve in pts with OSA only after several months of CPAP use
  - B. Has not been shown to markedly improve in pts with OSA
  - C. Has been shown to markedly improve in pts with OSA after 2 days of therapy with CPAP