Obstructive sleep apnea and obesity

Benjamas Intarapoka, MD.

Obstructive sleep apnea (OSA)

ICSD: diagnosis and coding manual; ASDA.1990

Apnea-Hypopnea Index (AHI) : mean of AH/ hr of sleep

EDS who had AHI > 5 /hr: 4% in male, 2% in female

Young T et al. N Eng J Med 1993

Repetitive Apnea

Sleep fragmentation/ sleep loss

Excessive daytime sleepiness

Neuro-cognitive: cognitive, vigilance, performance, personality, productivity, attention: acute reaction time (accident)

Sleep fragmentation, loss, insufficiency, deprivation

Repetitive Apnea

Sleep fragmentation

Hypoxia / hypercapnea

Excessive daytime sleepiness

CVS complications

Neuro-cognitive: cognitive, vigilance, performance, personality, productivity, attention, acute reaction time (accident)

HT, IHD, LVF, Pul HT and RVF

Stroke

Diagnostic criteria

Apnea: cessation of airflow ≥ 10 seconds
Hypopnea: decrease airflow ≥ 10 seconds

- Arousals
- \( O_2 \) desaturation

Normal \( \text{AHI or RDI} \) < 5
Mild 5-15
Moderate 15-30
Severe > 30

"Day time consequences"

Suggestive history

- Interruptive loud snoring
- Gasping / snorting / choking / "Restless sleep"
- Witness respiratory pauses
- Insomnia
- Nocturia / wet bed
- Un-refresh/ tired / pain / morning awakening
- AM headache / dizziness
- Day time sleepiness

"Bed partner"

409 PSG: Child 24 / adult 385
- Snoring: OSA 53 / 332 (1:6): loud/ intermittent
- Self-reported snoring 154/269 (60%)
- OSA: 332 M : F 274 : 58 (5:1)
- Age 48.5 yo (M 47.7 : F 53.0): post menopause
- Witness RS pauses 186/257 (72%)
- Self-reported apnea 137/266 (52%)
- Gasping / choking 222/258 (86%)

- AM headache 51%
- EDS: 89% (ESS > 10: 62.5%)
- Memory: 67%
- Accident related: 30%
- BMI 31.5 (STDE 7.8)
**Underlying or co-morbid diseases**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sedative used</td>
<td>20/266</td>
<td>(7%)</td>
</tr>
<tr>
<td>IHD</td>
<td>28/272</td>
<td>(10%)</td>
</tr>
<tr>
<td>DM</td>
<td>54/270</td>
<td>(20%)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>81/271</td>
<td>(30%)</td>
</tr>
<tr>
<td>HT</td>
<td>130/273</td>
<td>(48%)</td>
</tr>
<tr>
<td>Obesity</td>
<td>153/271</td>
<td>(56%)</td>
</tr>
<tr>
<td>Allergic rhinitis</td>
<td>181/274</td>
<td>(66%)</td>
</tr>
</tbody>
</table>

**Neck circumference**

<table>
<thead>
<tr>
<th>Category</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male ≤ 40 cm</td>
<td>103/218</td>
<td>(47%)</td>
</tr>
<tr>
<td>&gt; 40 cm</td>
<td>115/218</td>
<td>(53%)</td>
</tr>
<tr>
<td>Female ≤ 38 cm</td>
<td>35/53</td>
<td>(41.2%)</td>
</tr>
<tr>
<td>&gt; 38 cm</td>
<td>19/53</td>
<td>(37.9%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>BMI</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;25 kg/m²</td>
<td>46/279</td>
<td>(16%)</td>
</tr>
<tr>
<td>25 - &lt;30</td>
<td>92/279</td>
<td>(33%)</td>
</tr>
<tr>
<td>≥ 30</td>
<td>141/279</td>
<td>(51%)</td>
</tr>
<tr>
<td>≥ 40</td>
<td>40/279</td>
<td>(14%)</td>
</tr>
</tbody>
</table>

**ABG:**

pH 7.3 PaCO2 47 PaO2 58
O2 saturation room air 84%

Obesity hypoventilation syndrome
Pickwickian syndrome

Obese patient who had awake hypoventilation
- 10% in sleepy obese patients
- 50% of OSA (upper airway obstruction) who had MBI > 40

Sleep-related non-obstructive alveolar hypoventilation
- Central: obesity (BMI ≥ 35)
- neuromuscular and chest wall disease
- hypoventilation (PaCO₂ increase > 10, > 45 or O₂ desaturation with no apnea or hypopnea)

Obesity hypoventilation syndrome (OHS)

- Pickwickian syndrome
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OHS  50 cases

- M: F 31: 19
- Age 15- 80 (mean, median 49)
- ET/ TT 6 (12 %)
- Cyanosis 16 (32 %)
- Orthopnea 35 (70 %)
- Dyspnea 35 (70 %)
- EDS 100 %

Obese 43 (Mean 39.6) & OSA 31
Mean NC 42.7 cm
Underlying :
- DM 23
- HT 35
- Hyperlipidemia 23
- Allergic rhinitis 33
Reported snoring 45
Witness respiratory pauses 40
AM headache 28, Nocturia (>2) 35

Spectrum of SBD

OHS
Severe OSA
Moderate OSA
Mild OSA
Upper airway resistance syndrome 
(UARS)
Chronic heavy snorer
Intermittent snoring
Quiet breathing

Epidemic obesity

- 35.7% of USA adults are obese
- 16.9% of USA children & adolescents were obese 
  (18.6% boy, 15% girl)
- More prevalence in elderly (≥ 60 yo)
- Prevalence was the same between men & women
CDC/ NCNS, 2009- 2010
Thai12-18 yo KK 13.7% obese/ 5.3% over weight
Asian biomed 2010
Thai: university colleague Thai 36.9% M 16.7% F 2009

Upper airway of normal and obese patient
Sleep disordered breathing

- Sleep study (polysomnography) is gold standard for diagnosis and choice Tx
- Choice of treatment for any degree of severity is positive airway pressure (PAP)
- Weight reduction: diet control, exercise, lifestyle change, drugs and surgery for obese OSA

Other treatments

- Upper airway structure/ anatomical defect: Nose/ tonsils
- Positional treatment
- Oral appliances: mandibular advancement/ tongue retaining device
- Hypogossal nerve stimulation
- Negative pressure device
- Positive pressure device
- Drugs
- O2 therapy

UAR during oral & nasal breathing while awake and sleep


Other treatments

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- Positional treatment
- Oral appliances: mandibular advancement/ tongue retaining device
- Hypogossal nerve stimulation
- Negative pressure device
- Positive pressure device
- Drugs
- O2 therapy
Repetitive Apnea

Sleep fragmentation  Hypoxia/ hypercapnea

Metabolic dysregulation: IGT\(^1\), insulin resistance\(^{1,2}\) and DM\(^3\), decrease leptin, increase ghrelin level, increase hunger and appetite\(^4\).

1. Speigel. Lancet 1999
2. Panjabi. AJRCCM 2001
3. Yaggi; Diabetes Care 2006

Metabolic syndrome (Syndrome X)
Sleep apnea syndrome (Syndrome Z)

- High triglyceride
- Low HDL
- Central obesity
- Hypertension
- Insulin resistance
- Cyclic hypoxia
- Nocturnal sympathetic activation
- Sleep loss

Cardiovascular complications

OSA “syndrome Z”
- Common
- Serious cardiovascular complications
- OSA is one of diabetes risk factor which can be modified to reduce + prevent DM and cardio-vascular morbidities and mortality (treatable)
- IDF consensus statement on OSA and type 2 DM: awareness + practice

Meta-Analysis of short sleep duration and obesity in children and adults
Francesco P. Cappuccio et al. Sleep. 2008

1910: normal sleep duration was 9 hr
2000: normal sleep duration was 7.5 hr

Sleep fragmentation, loss, insufficiency, deprivation
Obstructive sleep apnea among obese patients with type 2 Diabetes

- The Sleep AHEAD research group
- 16 centers: 5145 over wt and obese
- Exclude treated OSA
- Un-attend PSG in 306 obese DM
  - 86% AHI ≥ 5 (mean 20.5±16.8)
  - 30.5% AHI 15-30
  - 22.6% AHI > 30
- WC was significant related to the presence of OSA
- Severe OSA had higher BMI

*Diabetes Care* 2009. 32(6):1017-1019

Share common factors

- Epidemic obesity: prevalence of disease
- One fourth in adults/ 56% of obese are at risk for OSA
- OSA in DM was 23%/ 6% in normal
  (West et al. *Thorax* 2006)
- OSA > 75% in obese DM
  (Foster et al. *Sleep* 2005)
- Both impact on CVD:MB +MR

OSA and diurnal hypertension

<table>
<thead>
<tr>
<th>Apnea hypopnea index</th>
<th>Adjusted* odd ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Reference</td>
</tr>
<tr>
<td>&gt; 0 - &lt; 5</td>
<td>1.42</td>
</tr>
<tr>
<td>≥ 5 - &lt; 15</td>
<td>2.03</td>
</tr>
<tr>
<td>≥ 15</td>
<td>2.89</td>
</tr>
</tbody>
</table>

* Adjusted for baseline hypertension, age, gender, BMI, WC, alcohol and tobacco use

*Peppard; NEJM 2000*

The JNC 7 report

- Identifiable causes of hypertension
  - Sleep apnea
  - Drug-induced or drug-related
  - Chronic kidney disease
  - Primary aldosteronism
  - Renovascular disease
  - Chronic steroid therapy and Cushing syndrome
  - Pheochromocytoma
  - Coarctation of aorta
  - Thyroid or parathyroid disease

Joint National Commission: JAMA 2003
Sleep duration predicts mortality

Sleep 2004; 27; 51-4

Sleep apnea and Cardiovascular disease

- Hypertension
- Heart failure
- Stroke
- Arrhythmia
- Myocardial ischemia and infarction
- Pulmonary artery hypertension
- End stage renal disease

JACC 2010

Intra-abdominal pressure, sagittal abdominal diameter and obesity comorbidity

SQUAREMAN A, WATSON M, BENSEN RL, WOOD

Table 1: Sagittal abdominal diameter and urinary bladder pressure in morbidly obese versus non-obese subjects (n=10)

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>BPD (cm)</th>
<th>SBP (mm Hg)</th>
<th>Bladder pressure (cm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morbidly obese patients (n=14)</td>
<td>11 ± 4</td>
<td>55 ± 1</td>
<td>51 ± 0.7</td>
</tr>
<tr>
<td>Normal weight patients (n=7)</td>
<td>62 ± 6</td>
<td>24 ± 2</td>
<td>19 ± 3.6</td>
</tr>
</tbody>
</table>

*P < 0.001
**BMI, body mass index; SBP, sagittal abdominal pressure.
OSA is one of cardiovascular risk factor

- HT (definite)
- Stroke (may be)
- Myocardial infarction (may be)
- Metabolic syndrome
- DM

High risk should be evaluated for OSA symptoms

- Obese (BMI > 35)
- CHF, AF, refractory HT, Nocturnal dysrhythmia
- DM type 2
- Stroke
- Preoperative for bariatric surgery
- Unexplained noxia
- Morning or nocturnal headache
- High risk driving population

Prevalence of unrecognized OSA

- Co-morbid conditions in 1,157 Australian:
  - Obese (BMI >30): 35%
  - Type 2 DM: 16%
  - Treated HT: 395
  - IHD: 5%
  - Mean ESS 8.3/24
- Mean age 53 yo (M/F 62/38%)
  - AHI > 5: 51%
  - AHI > 15: 33%
  - AHI > 30: 16%


STOP-Bang questionnaire

1. Snoring
2. Tired/ EDS
3. Observed apnea
4. Blood pressure
5. BMI
6. Age > 50
7. Neck circumference
8. Gender: male

AHI ≥ 5/hr : ≥ 3/8

Chung P et al. STOP Questionnaire- A tool to screen patients for OSA. Anesthology 2004; 100:822-30

Cardiovascular and metabolic effect of CPAP in OSAHS

- Blood pressure
- Insulin resistance
- DM
- Lipid profile
- Inflammatory mediators: IL6, CRP, TNF, NO
  - Eur Respir J 2007
  - JCSM 2008

The New England Journal of Medicine

CPAP for the Metabolic Syndrome in Patients with Obstructive Sleep Apnea

Sumendra K. Sharma, M.D., Ph.D., Swathi Agarwal, M.D., Deepak Dharshakumar, M.D., Vishalshada Srinivas, M.D., Tamilselvi Kathiresan, M.D., Ramakrishna Laxman, M.D., Priy Jagi, M.D., and Akin Kumar, M.D.
Table: Effects of CYP3A4 on the Concentration of the Metabolite, Metyrapone.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Treatment Effect</th>
<th>Difference or Odds Ratio (95% CI)</th>
<th>P Value</th>
</tr>
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<tbody>
<tr>
<td><strong>CYP3A4 (n=6)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minimal clearance</td>
<td>0.36</td>
<td>0.24</td>
<td>0.03</td>
</tr>
<tr>
<td>Symptomatic response</td>
<td>0.45</td>
<td>0.38</td>
<td>0.08</td>
</tr>
<tr>
<td>Duration of response</td>
<td>0.36</td>
<td>0.24</td>
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This table shows the effects of CYP3A4 on the concentration of the metabolite, metyrapone, in a study involving two groups. The table includes variables such as minimal clearance, symptomatic response, and duration of response, with corresponding difference or odds ratios and p-values. The results indicate a significant effect of CYP3A4 on these variables, suggesting that the enzyme plays a role in the metabolism of metyrapone.
Important points

• No diagnostic criteria
• Sleep study is gold standard for diagnosis
• Diet control, exercise and life style change
• Weight reduction surgery would get rid of obesity and its complications in severe morbid obesity
• No relation between BW reduction & AHI
• Sleep study is needed to before quit using CPAP