Sleep Apnea & Cardiovascular Disease

Jonathan A. Marcus MD
Assistant Professor of Neurology
UR MEDICINE Sleep Center
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Disclosures

SLEEP CHARACTERISTICS
HOW THEY VARY AND REACT TO CHANGING CONDITIONS IN THE GROUP AND THE INDIVIDUAL

N. KLEITMAN
F. J. MULLIN
N. R. COOPERMAN
S. TITELBAUM

The Department of Physiology of the University of Chicago

SLEEP CHARACTERISTICS

This investigation was aided by a generous grant from the Vanderbilt Company of Chicago, the manufacturers of Ovatis, one of the materials whose effect on the quality of sleep was studied among several others. To avoid any misunderstandings, we wish to state that we took the initiative in approaching Mr. James O. McEldowny, the president of The Vanderbilt Company, with the request for financial support for the investigation of the relationship of the different sleep characteristics and their modification by external and internal conditions. The grant was then made to the University of Chicago, subject to the usual rules formulated by the University for accepting aid for research from commercial concerns as regards the type of problem and the manner of publication, namely, that the problems involved should be of fundamental academic interest and that

the University reserves the right to decide whether the results should be published, and if published, the place, time, and method of publication.

It is expressly noted that publication will not depend upon relation of the results to the claims made by the donor, but upon general academic interest.

Mr. McEldowny, with the cooperation of his company, is making a complete study of the question of sleep as related to the use of Ovatis and will, it is hoped, publish a complete report on the subject at an early date.

We take this opportunity to express our thanks to the officers of the Vanderbilt Company for making this research possible. Thanks are also due to the Eli Lilly Company and the Winthrop Chemical Company for the generous supply of Ampit and Eripal, respectively, which we received from them. While we are not going to mention each subject by name, we wish to thank our human "pilates pigs" collectively for their loyalty and cooperation in the gathering of the data.

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Sleep Apnea & Cardiovascular Disease

• Defining Sleep Disordered Breathing
• Pathophysiology of Obstructive Sleep Apnea
• Evaluation/Work Up of Obstructive Sleep Apnea
• Impact of Obstructive Sleep Apnea on Cardiovascular Risk
• Impact of the Treatment of Obstructive Sleep Apnea on Cardiovascular Risk
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Sleep Disordered Breathing

• **Obstructive Sleep Apnea:**
  • Defined by repetitive episodes of upper airway obstruction during sleep causing arousals and leading to daytime sleepiness.

• **Upper Airways Resistance Syndrome:**
  • Condition in which increased upper airways resistance leads to frequent arousals but no apneas or hypopneas. The arousals cause daytime sleepiness.

• **Central Sleep Apnea:**
  • Defined by repetitive episodes during which there is cessation of respiratory effort, leading to disturbed sleep.
Sleep Disordered Breathing

• **Complex Sleep Apnea:**
  • Development of central sleep apnea in a patient with obstructive sleep apnea when treated with PAP therapy.

• **Obesity Hypoventilation Syndrome:**
  • Seen in obese patients, characterized by insufficient sleep-related ventilation resulting in elevated PaCO$_2$ not attributed to underlying cardiopulmonary or neuromuscular disease.
Obstructive Sleep Apnea (OSA)

OSA is defined by repetitive episodes of upper airway obstruction during sleep causing arousals and leading to daytime sleepiness.

**Common Symptoms:**
- Snoring
- Gasping/Choking Arousals
- Fragmented Sleep
- Non refreshing sleep (wake up tired)
- Morning dry mouth/headaches
- Nocturnal sweatiness/overheated
- Poor daytime concentration
- Irritability
- Erectile Dysfunction/Decreased Libido
- Nocturia
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OSA and Cardiovascular Disease
Summary of Possible Mechanisms

Pathophysiological effects of obstructive sleep apnea on the cardiovascular system
PNA=parasympathetic nervous system activity, PO$_2$=partial pressure of oxygen, PCO$_2$=partial pressure of carbon dioxide, SNA=sympathetic nervous system activity.
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Evaluation of Sleep Apnea 1980-2014ish
Evaluation of Sleep Apnea 2015-?
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Impact of OSA on Cardiovascular Risk

OSA

Hypertension
Stroke
CHF
Inflammation
Sympathetic Activation
LV afterload
Metabolic dysregulation

Atrial fibrillation
CAD
Sudden cardiac death
Oxidative stress
Increased coagulability
Endothelial dysfunction

Leptin
Obesity
Insulin resistance

CHEST 2008; 133:(793–804)
Impact of OSA on Hypertension

• **Nondipping Pattern:**
  • OSA is associated with lack of the normal pattern of reduction of blood pressure during sleep (ie, nondipping pattern).\(^1\)

• **OSA is a risk factor for the new onset of systemic hypertension:**
  • *Mild OSA* $\rightarrow$ OR of 2.0 of developing over a 4 year period.
  • *Moderate or severe OSA* $\rightarrow$ OR of 2.89\(^2\)

• **Resistant Hypertension:**
  • *OSA seen in 71% of patients with resistant htn* (BP>14/90, on 3 agents including diuretic)
  • *OSA seen in 38% of patients with controlled htn* (on at least one agent)
  • Think about undiagnosed OSA in patients with resistant hypertension.\(^3\)

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Impact of Treatment of OSA on Hypertension

- **Treatment with CPAP leads to a modest reduction in BP**¹
  - Mean drop of systolic BP by 2.6 ± 0.6 mm Hg (P<.001)
  - Mean drop of diastolic BP by 2.0 ± 0.4 mm Hg (P<.001)
  - Though small, this can still be meaningful in terms of cardiovascular end points.

- **Comparison of CPAP vs. Anti-hypertensive agent**²
  - CPAP decreased 24-hour mean BP by -2.1 ± 4.9 mm Hg (P<.001)
  - Valsartan 160 mg decreased 24 mean BP by -9.1 ± 7.2 mm Hg (P<.001)

- **Excessive daytime sleepiness matters with this issue.**
  - Most trials that looked at patients found to have OSA on screening, who were not tired by self report, had reduced benefit with regards to BP improvement with institution of CPAP.

Impact of OSA on Atrial Fibrillation

• **Increased Prevalence of Afib in OSA patients:**
  - *Individuals with severe OSA have OR 2-4 higher of having complex arrhythmias than those without OSA (even after adjustment for potential confounders).*
  - *The risk of OSA in Afib patients has been estimated to be between 30-80%.*

• **OSA may increase risk of recurrent Afib:**
  - *Meta Analysis: A diagnosis of OSA increased risk of recurrent AF after radiofrequency catheter ablation by 25%.*

• **OSA may be a modifiable risk factor for recurrent Afib (albeit data is limited)**

2. Chest. 2004;125(3):87
Impact of OSA on Pulmonary Hypertension

Prevalence of pulmonary hypertension is elevated in patients with OSA:

- In patients without comorbid lung disease, 20% were found to have mild pulm HTN on right heart cath.\(^1\) This finding has been replicated several times.


Survival in OSA patients with and without PH

Kaplan-Meier survival estimates in 83 patients with OSA with and without PH. The survival rate at 1, 4, and 8 y was 100%, 90%, and 76% in the non-PH group and 93%, 75%, and 43% in the PH group, respectively. PH = pulmonary hypertension.

*Am J Cardiol.* 2009;104(9):1300-1306
Conclusions

• Sleep Disordered Breathing is a common problem.

• OSA leads to changes in hemodynamic, autonomic, inflammatory, and metabolic pathways.

• We are increasingly using home sleep apnea tests to evaluate patients today.

• OSA seems to have a strong association with hypertension, particularly patients with resistant hypertension. CPAP therapy leads to a modest reduction in BP.

• OSA is more common in patients with Afib. Rx with CPAP may reduce risk of recurrent Afib following cardioversion.

• Pulmonary hypertension is more common in patients with OSA, and OSA may be a risk factor for the development of pulmonary hypertension.
Sweet Dreams & Thanks for Your Attention
Medicine of the Highest Order