The Impact of Sleep Disordered Breathing in our Allergy/Immunology Patients

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Faculty Disclosure Information
Bradley Chipps, MD

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- I **do not** intend to discuss an unapproved/investigative use of a commercial product/device in my presentation.
Learning Objectives

- Understanding the historic and physiologic diagnostic criteria for sleep apnea from infancy to adults.
- Define risk of untreated sleep apnea.
- Identifying treatment options for sleep apnea.
### Definitions of obstructive sleep disordered breathing and its clinical entities

<table>
<thead>
<tr>
<th>Obstructive sleep disordered breathing (SDB)</th>
<th>A syndrome of upper airway dysfunction during sleep characterised by snoring and/or increased respiratory effort that result from increased upper airway resistance and pharyngeal collapsibility</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Obstructive SDB clinical entities</strong></td>
<td></td>
</tr>
<tr>
<td>Primary snoring</td>
<td>Habitual snoring (&gt;3 nights per week) without apnoeas, hypopnoeas, frequent arousals from sleep or gas exchange abnormalities</td>
</tr>
<tr>
<td>Upper airway resistance syndrome</td>
<td>Snoring, increased work of breathing, frequent arousals, but no recognisable obstructive events or gas exchange abnormalities</td>
</tr>
<tr>
<td>Obstructive hypoventilation</td>
<td>Snoring and abnormally elevated end-expiratory carbon dioxide partial pressure in the absence of recognisable obstructive events</td>
</tr>
<tr>
<td>Obstructive sleep apnoea syndrome</td>
<td>Recurrent events of partial or complete upper airway obstruction (hypopnoeas, obstructive or mixed apnoeas) with disruption of normal oxygenation, ventilation and sleep pattern</td>
</tr>
</tbody>
</table>

Which of the following is most predictive of an OSA diagnosis?

- a) Male gender
- b) Age > 55 years old
- c) Neck size > 17 inches
- d) BMI > 30 Kg/m²
## Risk Factors for Obstructive Sleep Apnea

<table>
<thead>
<tr>
<th>Non-modifiable risk factors</th>
<th>Modifiable risk factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increasing age (&gt;40 y)</td>
<td>Obesity (BMI &gt;35 kg/m²)</td>
</tr>
<tr>
<td>Male sex</td>
<td>Large neck size (&gt;16 inches in women, &gt;17 inches in men)</td>
</tr>
<tr>
<td>Postmenopausal state</td>
<td>Alcohol intake</td>
</tr>
<tr>
<td>Race (African American, Asian)</td>
<td>Smoking</td>
</tr>
<tr>
<td>Congenital craniofacial abnormality</td>
<td>Hypothyroidism</td>
</tr>
<tr>
<td>Type 1 diabetes₆⁵</td>
<td>Acromegaly</td>
</tr>
<tr>
<td>ESRD₆⁶</td>
<td>Enlarged tonsils and adenoids</td>
</tr>
<tr>
<td>Structural abnormality of nasal and oropharynx₆⁷</td>
<td></td>
</tr>
</tbody>
</table>
The NoSAS score for screening of sleep-disordered breathing: a derivation and validation study

<table>
<thead>
<tr>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neck circumference &gt;40 cm</td>
</tr>
<tr>
<td>Obesity</td>
</tr>
<tr>
<td>BMI 25 kg/m² to &lt;30 kg/m²</td>
</tr>
<tr>
<td>BMI ≥30 kg/m²</td>
</tr>
<tr>
<td>Snoring</td>
</tr>
<tr>
<td>Age &gt;55 years</td>
</tr>
<tr>
<td>Sex: male</td>
</tr>
</tbody>
</table>

The patient has a high probability of sleep-disordered breathing if they have a NoSAS score of 8 or higher. BMI = body mass index.

*Table 2: NoSAS score*

Clinical Evaluation in Predicting Childhood Obstructive Sleep Apnea

- 50 patients 4-18 years old – referral to PSG
- OSA = AHI > 5
- Primary snoring = AHI < 5
- 6 factors, 93% predicted
  - Observable apnea
  - Enuresis
  - Intrusive naps
  - Mouth breathing
  - Enlarged tonsils
  - X-ray adenoid enlargement

Prevalence of sleep apnoea syndrome in the middle to old age general population

Upper airway and systemic inflammation in obstructive sleep apnoea

What percentage of extra thoracic resistance is contributed by nasal airway?

- a) 15 %
- b) 25 %
- c) 35 %
- d) 50%
Inspiratory flow through the upper airway promotes closure of the airway

The tethered upper airway and forces that keep it patent during changes in internal pressures associated with respiration

Interactions of obstructive sleep apnoea and obesity in the development of cardiovascular and metabolic comorbidities

Contrasting prevalence of mild obstructive sleep apnoea based on sleep-disordered breathing alone where associated daytime clinical features are included.

- SAR
- PAR
Nasal Congestion in Patients with SAR is Associated with Obstructive Sleep Apneas*

*5 men with SAR.


Increase in obstructive sleep apneas/hour

Increase in nasal resistance (%)
Impaired Sleep in Patients with Allergic Rhinitis

Craig JACI 2007.
Allergic Rhinitis Symptoms are Associated with *Sleep Complaints*


<table>
<thead>
<tr>
<th>Sleep Complaint</th>
<th>Controls (n=502)</th>
<th>AR Patients (n=591)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Difficulty Falling Asleep</td>
<td>18.3%</td>
<td>20.5%</td>
</tr>
<tr>
<td>Nocturnal Awakening</td>
<td>41.6%</td>
<td>42.8%</td>
</tr>
<tr>
<td>Early Awakening</td>
<td>12.8%</td>
<td>28.7%</td>
</tr>
<tr>
<td>Nonrestorative Sleep</td>
<td>19.6%</td>
<td>46.8%</td>
</tr>
<tr>
<td>Feeling of Lack of Sleep</td>
<td>25.4%</td>
<td>63.2%</td>
</tr>
<tr>
<td>Snoring</td>
<td>27.1%</td>
<td>40.3%</td>
</tr>
<tr>
<td>ESS score &gt;10</td>
<td>17.2%</td>
<td>23.3%</td>
</tr>
</tbody>
</table>

*P<0.001 vs controls.*

Allergic Rhinitis Symptoms are Associated with *Sleep Disorders*

Prevalence of *Sleep Disorders* in Patients with Allergic Rhinitis and Controls

- **Insomnia**
  - Controls (n=502): 16%
  - AR Patients (n=591): 35.8%
  - *P* ≤ 0.003 vs controls.

- **Severe Insomnia**
  - Controls (n=502): 10.4%
  - AR Patients (n=591): 23.2%
  - *P* ≤ 0.003 vs controls.

- **Sleep Apnea Syndrome**
  - Controls (n=502): 0.5%
  - AR Patients (n=591): 3.8%
  - *P* ≤ 0.003 vs controls.

- **Hypersomnia**
  - Controls (n=502): 24.3%
  - AR Patients (n=591): 32.6%

*P* ≤ 0.003 vs controls.

Multiple Pro-Inflammatory Factors in Allergic Rhinitis Affect Sleep and Symptoms

<table>
<thead>
<tr>
<th>Mediator</th>
<th>Effect on Sleep</th>
</tr>
</thead>
<tbody>
<tr>
<td>Histamine</td>
<td>Balance between wakefulness and sleep, arousal; ↑ nasal obstruction, rhinorrhea, &amp; pruritus</td>
</tr>
<tr>
<td>CysLT</td>
<td>↑ Slow-wave sleep, ↑ Sleep-disordered breathing; ↑ Nasal obstruction, rhinorrhea</td>
</tr>
<tr>
<td>IL-1</td>
<td></td>
</tr>
<tr>
<td>IL-4</td>
<td>↑ Latency to REM and ↓ REM duration</td>
</tr>
<tr>
<td>IL-10</td>
<td></td>
</tr>
<tr>
<td>Bradykinin</td>
<td>↑ Sleep apnea; ↑ Nasal obstruction &amp; rhinorrhea</td>
</tr>
<tr>
<td>Substance P</td>
<td>↑ Latency to REM, arousal; ↑ Nasal obstruction</td>
</tr>
</tbody>
</table>

Sleep Apnea & Performance
Allergic Rhinitis Impairs Learning in Pediatric Patients

Mean Learning Scores in Children 10-12 Years of Age (N=73)

* $P=0.007$ vs healthy controls.
† $P=0.002$ vs healthy controls.

Impact of Poor Sleep

- Delayed onset
- Sleep fragmentation
  - Arousals/microarousals
- Sleep Disordered Breathing
  - Snoring
  - Obstructive Sleep Apnea

Impaired Social Functioning:
- daytime fatigue/somnolence
- Impaired performance
- Impaired learning
- Emotional/behavioral impact

Associated Diseases:
- Hypertension
- Cardiovascular disease
- Stroke
- Diabetes
- Psychological disorders
Habitual Snoring is Associated with Poor Academic Performance in Primary School Children

**Odds Ratio** for Poor Performance by Snoring Category

- **Snoring Category**
  - Never
  - Occasionally
  - Frequently
  - Always

**Mathematics**
- *Never*: 2
- *Occasionally*: 2
- *Frequently*: 4
- *Always*: 4

**Science**
- *Never*: 2
- *Occasionally*: 2
- *Frequently*: *6
- *Always*: *6

**Spelling**
- *Never*: 2
- *Occasionally*: 2
- *Frequently*: *6
- *Always*: *6

*\( P \leq 0.038 \) vs never.

Sleep-Disordered Breathing Increases Risk of Psychiatric Disorders

Incidence of Psychiatric Disorders in Patients without and with Diagnosed Sleep Apnea†

*P<0.001 vs no apnea. PTSD=post-traumatic stress disorder.
†Apnea defined by diagnosis of sleep apnea associated with insomnia, hypersomnia, or other unspecified.
Sleep-Disordered Breathing Increases Risk of Behavioral Problems in Children

Prevalence of Behavioral Problems According to Sleep-Disordered Breathing

* \( P \leq 0.01 \) vs no SDB.

OSA & Asthma

A Bidirectional Relationship
# Adjusted Relative Risks for Asthma and Asthma Duration Predicting 4-Year Incidence of Obstructive Sleep Apnea

<table>
<thead>
<tr>
<th>Incident OSA(^a)</th>
<th>Incident OSA + Habitual Sleepiness(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RR (95% CI)</td>
<td>P Value</td>
</tr>
<tr>
<td>---------------------</td>
<td>------------------------------------------</td>
</tr>
<tr>
<td>Model 1: any asthma vs no asthma(^c)</td>
<td></td>
</tr>
<tr>
<td>No asthma</td>
<td>1 [Reference]</td>
</tr>
<tr>
<td>Any asthma</td>
<td>1.39 (1.06-1.82)</td>
</tr>
<tr>
<td>Model 2: continuous duration of asthma(^c)</td>
<td></td>
</tr>
<tr>
<td>Duration (5-y increments)</td>
<td>1.07 (1.02-1.13)</td>
</tr>
<tr>
<td>Model 3: duration of asthma categories(^c)</td>
<td></td>
</tr>
<tr>
<td>No asthma</td>
<td>1 [Reference]</td>
</tr>
<tr>
<td>Short duration (≤10 y)</td>
<td>1.06 (0.67-1.67)</td>
</tr>
<tr>
<td>Long duration (&gt;10 y)</td>
<td>1.65 (1.21-2.25)</td>
</tr>
<tr>
<td>P value for trend in RRs</td>
<td>.008</td>
</tr>
</tbody>
</table>

Teodorescu M et al. JAMA 2015;313(2) : 156-16.
Association of Obstructive Sleep Apnea Risk With Asthma Control in Adults

Kaplan–Meier survival curves for (A) FEV1 and (B) apnea–hypopnea index (AHI) categories.

Sleep apnea is associated with bronchial inflammation and continuous positive airway pressure–induced airway hyperresponsiveness

Nonspecific airway responsiveness to methacholine expressed as PD20 in patients with OSA before and after 1 and 4 weeks of CPAP therapy

Sleep-Disordered Breathing is Associated with Asthma Severity in Children

- 108 patients - mean age, 9.1 ± 3.4 years;
- 45.4% African-American; 67.6% male
- Obesity 42.6%; SDB 29.6%
- Odds ratio- 3.62 severe asthma
- SDB determined by loud snoring and > 3 desaturations /hr

The most effective pharmacologic treatment for primary snoring and OSA in children are?

- a) Intranasal Corticosteroids (INS)
- b) Topical alpha agonist
- c) Montelukast (MTL)
- d) INS and MTL
Leukotriene Receptor Antagonists

AR Symptoms

Inflammation

Congestion

Impaired Sleep
Leukotriene Modifier Therapy for Mild Sleep-disordered Breathing in Children

Lateral neck soft X-ray in a 6-year-old patient with mild sleep disordered breathing before (Pre) and after (Post) 16-week course of montelukast.

Leukotriene Receptor Antagonists: Effect on Congestion and Sleep in Patients with SAR

Improvement in Total and Individual *Nighttime* Symptoms Over Placebo

- Percentage improvements over placebo were modest for both total and individual *nighttime* symptoms

*P* ≤ 0.003 vs placebo.

All symptoms were scored on a scale from 0 (best) to 3 (worst).

Intranasal Steroids (INS) Reduce Inflammation, AR Symptoms and Congestion and Improve Sleep

- AR Symptoms
- Inflammation
- Congestion
- Impaired Sleep
Intranasal Steroid Therapy Improves Symptoms, Sleep, and Quality of Life in Children with Allergic Rhinitis

Figure 2. Nasal symptoms on the Mini–Rhinitis Quality of Life Questionnaire. Statistical significance was as follows: sneezing, $F = 5.09$, $P = .005$; runny nose, $F = 2.27$, $P = .09$; and stuffy nose, $F = 8.40$, $P < .001$.

Adverse Impact of Allergic Rhinitis on the Patient Quality of Life-Focus on Sleep: Conclusions

- Allergic rhinitis is associated with impaired sleep
- Sleep impairment in allergic rhinitis can be caused by
  - Inflammatory mediators
  - Nasal symptoms, primarily congestion and rhinorrhea
  - Ocular symptoms
- Impaired sleep adversely affects performance, productivity and social functioning, and increases the risk of associated diseases
- Intranasal steroids effectively target inflammation and relieve symptoms to provide improved sleep
Effect of Therapies for Allergic Rhinitis on Sleep and Quality of Life: Summary

- Intranasal steroids provide significant relief of congestion and ocular symptoms and improve sleep in patients with allergic rhinitis
- Non-sedating antihistamines and leukotriene receptor antagonists provide modest improvements in congestion, ocular, and nighttime symptoms
- Nasal decongestants effectively reduce congestion, but have minimal affect on sleep-disordered breathing
Sleep and Atopic Dermatitis

- 14 atopic dermatitis patients (6 ± 2 years old) - in remission
- 9 controls (7 ± 2 years old)
- PSG, "scratch electrodes", sleep quantities
- AD 24.1 ± 8 events/hr
  Control 15.4 ± 6 events/hr
- Scratching only 15% of arousals
- No correlation with PSG

Conditional probability plot for sleep disturbance, eczema, and allergic disease within latent classes

Treatment
Adult OSA Treatment

1. Weight loss
2. ETOH - medication
3. Oral appliances
4. Sleep posture
5. CPAP/Bi-Level
6. Tracheostomy
CPAP for Prevention of Cardiovascular Events in Obstructive Sleep Apnea

![Graph showing cumulative incidence over follow-up periods for CPAP and usual care.]

**Cumulative Incidence (%)**

<table>
<thead>
<tr>
<th>No. at Risk</th>
<th>CPAP</th>
<th>Usual care</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>12</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>24</td>
<td>20</td>
<td>20</td>
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<td>36</td>
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<td>48</td>
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<td>40</td>
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<tr>
<td>60</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>72</td>
<td>60</td>
<td>60</td>
</tr>
<tr>
<td>84</td>
<td>70</td>
<td>70</td>
</tr>
</tbody>
</table>

P = 0.34

Children OSA Treatment

1. Weight loss
2. Oral appliances
3. INS/MTL
4. Surgical
Risk Factors for Postoperative Respiratory Complications in Children With OSAS Undergoing Adenotonsillectomy

<table>
<thead>
<tr>
<th>Younger than 3 y of age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe OSAS on polysomnography(^a)</td>
</tr>
<tr>
<td>Cardiac complications of OSAS</td>
</tr>
<tr>
<td>Failure to thrive</td>
</tr>
<tr>
<td>Obesity</td>
</tr>
<tr>
<td>Craniofacial anomalies(^b)</td>
</tr>
<tr>
<td>Neuromuscular disorders(^b)</td>
</tr>
<tr>
<td>Current respiratory infection</td>
</tr>
</tbody>
</table>

Are there conditions predisposing to upper airway obstruction which make treatment of obstructive SDB a priority?

Summary

- a) Major craniofacial abnormalities
- b) Neuromuscular disorders
- c) Achondroplasia
- d) Chiari malformation
- e) Down syndrome
- f) Mucopolysaccharidoses
- g) Prader–Willi syndrome

Thank You