Identification and Treatment of the Patient with Sleep Related Hypoventilation

Hillary Loomis-King, MD
Pulmonary and Critical Care of NW MI
Munson Sleep Disorders Center
Conflict of Interest Disclosures for Speakers

1. I do not have any relationships with any entities producing, marketing, re-selling, or distributing health care goods or services consumed by, or used on, patients, OR

2. I have the following relationships with entities producing, marketing, re-selling, or distributing health care goods or services consumed by, or used on, patients.

<table>
<thead>
<tr>
<th>Type of Potential Conflict</th>
<th>Details of Potential Conflict</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grant/Research Support</td>
<td></td>
</tr>
<tr>
<td>Consultant</td>
<td></td>
</tr>
<tr>
<td>Speakers’ Bureaus</td>
<td></td>
</tr>
<tr>
<td>Financial support</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td></td>
</tr>
</tbody>
</table>

3. The material presented in this lecture has no relationship with any of these potential conflicts, OR

4. This talk presents material that is related to one or more of these potential conflicts, and the following objective references are provided as support for this lecture:
Objectives

1- Understand basic pulmonary physiology and the mechanisms through which hypoxia and hypoventilation occur.
2- Establish patient populations in which hypoventilation needs to be considered.
3- Know diagnostic criteria for sleep-related hypoventilation syndromes.
4- Understand treatment options and qualifying criteria for patients with clinical hypoventilation.
PHYSIOLOGY OF VENTILATION
$V_E = V_T \times f$

Minute Ventilation: closely linked with blood CO$_2$ values.
Alveolar Anatomy

- Oxygen enters red blood cells
- Capillary
- Red blood cell
- Diffusion of oxygen
- To pulmonary vein
- Epithelium of alveolus
- Film of moisture
- Carbon dioxide escapes into alveolus
- From pulmonary artery
- Ventilation
Alveolar Ventilation

\[ \text{PaCO}_2 = \kappa \times \left( \frac{V_{CO_2}}{V_A} \right) \]

where

\[ V_A = V_E - V_E \left( \frac{V_D}{V_T} \right) \]
Alveolar Ventilation

$V_D = \text{dead space}$

Fixed dead space

Alveolar dead space
- VQ mismatch
  - Atelectasis, pulmonary embolism, pulmonary vascular disease, pneumonia
- R to L shunt
- Impaired Diffusion
  - Interstitial lung disease
Hypoxemia in Hypoventilation

\[ PAO_2 = (P_{atm} - P_{H_2O})FIO_2 - (P_{ACO_2}/RQ) \]

*Contribution of FIO\(_2\) in this equation shows why hypoxemia can be overcome by addition of supplemental oxygen.*
Renal Compensation

• Respiratory acidosis is buffered by renal compensation

\[ \text{CO}_2 + \text{HOH} \rightleftharpoons \text{H}_2\text{CO}_3 \rightleftharpoons \text{H}^+ + \text{HCO}_3^- \]
Pulmonary Function Testing

**Flow/Volume**

- Predicted
- Baseline

**Volume (Liters)**

---

<table>
<thead>
<tr>
<th>Oximetry at Rest: 95% at 0.21 FIO2</th>
</tr>
</thead>
</table>

**Baseline**

<table>
<thead>
<tr>
<th>LUNG MECHANICS</th>
<th>Actual</th>
<th>Pred</th>
<th>%Pred</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC (liters)</td>
<td>3.82</td>
<td>3.64</td>
<td>105%</td>
</tr>
<tr>
<td>FEV1 (liters)</td>
<td>3.16</td>
<td>2.84</td>
<td>111%</td>
</tr>
<tr>
<td>FEV1/FVC (%)</td>
<td>83%</td>
<td>78%</td>
<td>106%</td>
</tr>
<tr>
<td>FEV6 (liters)</td>
<td>3.82</td>
<td>3.71</td>
<td>103%</td>
</tr>
<tr>
<td>PEF (sec)</td>
<td>6.66</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEF25-75 (l/sec)</td>
<td>8.46</td>
<td>6.34</td>
<td>134%</td>
</tr>
<tr>
<td>FEF50 (l/sec)</td>
<td>3.33</td>
<td>3.26</td>
<td>102%</td>
</tr>
<tr>
<td>FIFMAX (l/sec)</td>
<td>3.62</td>
<td>3.64</td>
<td>99%</td>
</tr>
<tr>
<td>FIF50 (l/sec)</td>
<td>6.00</td>
<td>6.34</td>
<td>95%</td>
</tr>
<tr>
<td>FEF50/FIF50 (%)</td>
<td>5.43</td>
<td>4.53</td>
<td>120%</td>
</tr>
<tr>
<td>MVV (l/min)</td>
<td>121</td>
<td>107</td>
<td>114%</td>
</tr>
</tbody>
</table>

**LUNG VOLUMES**

<table>
<thead>
<tr>
<th>Actual</th>
<th>Pred</th>
<th>%Pred</th>
</tr>
</thead>
<tbody>
<tr>
<td>VC (liters)</td>
<td>3.85</td>
<td>3.64</td>
</tr>
<tr>
<td>IC (liters)</td>
<td>2.46</td>
<td>2.26</td>
</tr>
<tr>
<td>ERV (liters)</td>
<td>1.39</td>
<td>1.38</td>
</tr>
<tr>
<td>FRC pleth (liters)</td>
<td>3.30</td>
<td>2.84</td>
</tr>
<tr>
<td>RV pleth (liters)</td>
<td>1.91</td>
<td>1.46</td>
</tr>
<tr>
<td>TLC pleth (liters)</td>
<td>5.76</td>
<td>5.10</td>
</tr>
<tr>
<td>RV/TLC pleth (%)</td>
<td>33%</td>
<td>29%</td>
</tr>
</tbody>
</table>

**Raw cmH2O/l/s**

<table>
<thead>
<tr>
<th>Actual</th>
<th>Pred</th>
<th>%Pred</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sgaw s/cmH2O*l^2</td>
<td>0.26</td>
<td>&gt;0.21</td>
</tr>
</tbody>
</table>

**DIFFUSION**

<table>
<thead>
<tr>
<th>Actual</th>
<th>Pred</th>
<th>%Pred</th>
</tr>
</thead>
<tbody>
<tr>
<td>DLCO ml/min/mmHg</td>
<td>20.87</td>
<td>24.19</td>
</tr>
<tr>
<td>IVC (liters)</td>
<td>3.73</td>
<td>3.85</td>
</tr>
<tr>
<td>VA (liters)</td>
<td>5.25</td>
<td>5.10</td>
</tr>
<tr>
<td>DL/VA ml/m/Hzg/l</td>
<td>3.98</td>
<td>4.75</td>
</tr>
</tbody>
</table>
POPULATIONS TO CONSIDER
HYPOVENTILATION
Known Gas Abnormalities

- Sustained hypoxia on baseline study
- Supplemental oxygen requirement in wakefulness
- Prior ABG with pCO₂ > 45 mmHg

\[ P_{AO2} = (P_{atm} - P_{H2O})FIO2 - (P_{ACO2}/RQ) \]
Other Populations

- Lung disease
- Neuromuscular disease
- Chest wall disease
- Morbid obesity
- Elevated serum bicarbonate
- Polycythemia
Other Populations

• Lung disease
  – Increased dead space
• Neuromuscular disease
  – Decreased $V_T$
• Chest wall disease
  – Decreased $V_T$
• Morbid obesity
  – Decreased $V_T$, atelectasis and VQ mismatch
• Elevated serum bicarbonate
• Polycythemia
ESTABLISHING THE DIAGNOSIS OF HYPOVENTILATION
If electing to score hypoventilation, score hypoventilation during sleep if EITHER of the below occur:

a. There is an increase in the arterial PCO$_2$ (or surrogate) to a value $>55$ mmHg for $\geq10$ minutes.

b. There is $\geq10$ mmHg increase in arterial PCO$_2$ (or surrogate) during sleep (in comparison to an awake supine value) to a value exceeding 50 mmHg for $\geq10$ minutes.
Methodologies for Measuring CO$_2$

- Arterial Blood Gas
- End Tidal CO$_2$- non-invasive measurement of partial pressure of CO2 exhaled
- TCO2- CO2 is still measured potentiometrically by determining the pH of an electrolyte layer
ICSD-3: Sleep Related Hypoventilation Disorders

Categories

• Obesity Hypoventilation Syndrome
• Congenital Central Alveolar Hypoventilation Syndrome
• Late-Onset Central Hypoventilation with Hypothalamic Dysfunction
• Idiopathic Central Alveolar Hypoventilation
• Sleep Related Hypoventilation Dues to a Medication or Substance
• Sleep Related Hypoventilation Does to a Medical Disorder
ICSD-3: Obesity Hypoventilation Syndrome

Criteria A-C must be met

A. Presence of hypoventilation during wakefulness (PaCO$_2$ > 45 mmHg) as measured by arterial PCO$_2$, end-tidal CO$_2$, or transcutaneous CO$_2$

B. Presence of obesity (BMI > 30 kg/m$^2$)

C. Hypoventilation is not primarily due to lung parenchymal or airway disease, pulmonary vascular pathology, chest wall disorder, medication use, neurologic disorder, muscle weakness, or a known congenital or idiopathic central alveolar hypoventilation syndrome
ICSD-3: Congenital Central Alveolar Hypoventilation Syndrome

Criteria A & B must be met

A. Sleep related hypoventilation is present
B. Mutation of the PHOX2B gene is present
ICSD-3: Late-Onset Central Hypoventilation with Hypothalamic Dysfunction

Criteria A-E must be met
A. Sleep related hypoventilation is present
B. Symptoms are absent during the first few years of life
C. The patient has at least two of the following:
   1. Obesity
   2. Endocrine abnormalities of hypothalamic origin
   3. Severe emotional or behavioral disturbances
   4. Tumor of neural origin
D. Mutation of the \textit{PHOX2B} gene is not present.
E. The disorder is not better explained by another sleep disorder, medical or neurological disorder, medication use, or substance use disorder.
ICSD-3: Idiopathic Central Alveolar Hypoventilation

Criteria A & B must be met

A. Sleep related hypoventilation is present
B. Hypoventilation is not primarily due to lung parenchymal or airway disease, pulmonary vascular pathology, chest wall disorder, medication use, neurologic disorder, muscle weakness, or obesity or congenital hypoventilation syndromes.
ICSD-3: Sleep Related Hypoventilation Dues to a Medication or Substance

Criteria A-C must be met

A. Sleep related hypoventilation is present.
B. A medication or substance known to inhibit respiration and/or ventilatory drive is believed to be the primary cause of sleep related hypoventilation.
C. Hypoventilation is not primarily due to lung parenchymal or airway disease, pulmonary vascular pathology, chest wall disorder, neurologic disorder, muscle weakness, obesity hypoventilation syndrome, or known congenital central alveolar hypoventilation syndrome.
ICSD-3: Sleep Related Hypoventilation Dues to a Medical Disorder

Criteria A-C must be met

A. Sleep related hypoventilation is present
B. A lung parenchymal or airway disease, pulmonary vascular pathology, chest wall disorder, neurologic disorder, or muscle weakness is believed to be the primary cause of hypoventilation
C. Hypoventilation is not primary due to obesity hypoventilation syndrome, medication use, or a known congenital central alveolar hypoventilation syndrome
TREATMENT OPTIONS
E0470: Bi-level PAP

No back up rate, most algorithms require that a patient fail this prior to covering more advanced device.
E0471: Bi-level PAP with back-up rate

- Bi-level PAP with back up rate
  - Compared with traditional bi-level PAP, guarantees a minimal number of breaths per minute
  - Does not guarantee goal minute ventilation
E0471: AVAPS

Average Volume Assured Pressure Support

Settings

• Target $V_T$
• IPAP min & IPAP max
• EPAP (some devices now have adjusting EPAP)
• Breath rate
• Inspiratory time ($T_i$)
• Rise time
QUALIFYING CRITERIA
Restrictive Thoracic Disorders

Documentation of neuromuscular disease or severe thoracic cage abnormality in the patient’s medical record

Perform one of the following:
- ABGs (done while awake and on prescribed FiO₂) PaCO₂ ≥ 45 mm Hg or
- Sleep oximetry
  Oxygen saturation ≤ 88% for ≥ 5 minutes, minimum 2 hours of recording time (on patient’s prescribed FiO₂) or
- For neuromuscular disease only:
  Either FVC < 50% of predicted or MIP < 60 cm H₂O

(E0470) or (E0471)
Based on the treating physician’s judgment

COPD does not contribute significantly to pulmonary limitation
For COPD to qualify for E0471 device:

1) After initial period of use of E0470, ABG with PaCO₂ ≥ 7 mmHg higher than original ABG result or facility based PSG with O₂ saturation < 88% for > cumulative 5 minutes on E0470

2) No sooner than 61 days after initiation of E0470, ABG shows PaCO₂ ≥ 52 mmHg or sleep oximetry on E0470 demonstrates O₂ saturation , 88% for a cumulative > 5 minutes.
Hypoventilation

**ABGs** (done while awake and on prescribed FiO₂)
PaCO₂ ≥ 45 mm Hg

**Spirometry**
FEV₁/FVC ≥ 70%
Refer to SEVERE COPD category for information about device coverage for patients with FEV₁/FVC <70%

- **ABGs** (done during sleep or immediately upon awakening on prescribed FiO₂ show) PaCO₂ worsened ≥ 7 mm Hg compared to original ABG
- **PSG or HST** demonstrates oxygen saturation ≤ 88% for ≥ 5 minutes, minimum 2 hours nocturnal recording time not caused by obstructive upper airway events (ie, AHI < 5)

(E0470)
Hypoventilation, continued

Covered E0470 is being used

Spirometry
FEV1/FVC ≥ 70%
Refer to SEVERE COPD category for information about device coverage for patients with FEV1/FVC < 70%

- ABGs (done while awake and on prescribed FiO₂) PaCO₂ worsens ≥ 7 mm Hg compared to ABG result used to qualify for E0470 or
- PSG or HST demonstrates oxygen saturation ≤ 88% for ≥ 5 minutes, minimum 2 hours nocturnal recording time, and not caused by obstructive upper airway events (ie, AHI < 5 while on E0470)

(E0471)
32yo female with morbid obesity presents with subacute dyspnea and 30lb weight gain.

- ABG on 5L supplemental oxygen:
  - pH 7.37, pCO$_2$ 74, pO$_2$ 46, SpO$_2$ 76%
- Measured HCO$_3^-$: >40
# PFT- OHS (7/2011)

## Oximetry at Rest:
- $95\%$ at $0.21\, \text{FIO}_2$

### LUNG MECHANICS

<table>
<thead>
<tr>
<th></th>
<th>Actual</th>
<th>Pred</th>
<th>%Pred</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC (liters)</td>
<td>1.11</td>
<td>3.51</td>
<td>32%</td>
</tr>
<tr>
<td>FEV1 (liters)</td>
<td>0.96</td>
<td>2.79</td>
<td>34%</td>
</tr>
<tr>
<td>FEV1/FVC (%)</td>
<td>85%</td>
<td>79%</td>
<td>109%</td>
</tr>
<tr>
<td>FVC (liters)</td>
<td>1.11</td>
<td>3.49</td>
<td>32%</td>
</tr>
<tr>
<td>PEF (sec)</td>
<td>8.03</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PEFmax (l/sec)</td>
<td>3.59</td>
<td>6.22</td>
<td>58%</td>
</tr>
<tr>
<td>PEF25-75 (l/sec)</td>
<td>1.24</td>
<td>3.31</td>
<td>37%</td>
</tr>
<tr>
<td>FVC (liters)</td>
<td>0.93</td>
<td>3.51</td>
<td>26%</td>
</tr>
<tr>
<td>PEFmax (l/sec)</td>
<td>2.24</td>
<td>6.22</td>
<td>36%</td>
</tr>
<tr>
<td>PEF50 (l/sec)</td>
<td>2.23</td>
<td>4.53</td>
<td>49%</td>
</tr>
<tr>
<td>FEF50/FEF50 (%)</td>
<td>82%</td>
<td>100%</td>
<td>82%</td>
</tr>
<tr>
<td>MV (l/min)</td>
<td>45</td>
<td>106</td>
<td>43%</td>
</tr>
</tbody>
</table>

### LUNG VOLUMES

<table>
<thead>
<tr>
<th></th>
<th>Actual</th>
<th>Pred</th>
<th>%Pred</th>
</tr>
</thead>
<tbody>
<tr>
<td>VC (liters)</td>
<td>1.11</td>
<td>3.51</td>
<td>32%</td>
</tr>
<tr>
<td>IC (liters)</td>
<td>0.92</td>
<td>2.10</td>
<td>42%</td>
</tr>
<tr>
<td>ERV (liters)</td>
<td>0.19</td>
<td>1.32</td>
<td>14%</td>
</tr>
<tr>
<td>FRC pleth (liters)</td>
<td>1.30</td>
<td>2.02</td>
<td>50%</td>
</tr>
<tr>
<td>RV pleth (liters)</td>
<td>1.11</td>
<td>1.30</td>
<td>85%</td>
</tr>
<tr>
<td>TLC pleth (liters)</td>
<td>2.22</td>
<td>4.81</td>
<td>46%</td>
</tr>
<tr>
<td>RV/TLC pleth (%)</td>
<td>50%</td>
<td>27%</td>
<td>185%</td>
</tr>
<tr>
<td>Raw (cmH2O/l/s)</td>
<td>3.43</td>
<td>&lt;2.00</td>
<td></td>
</tr>
<tr>
<td>Sqaw (s/cmH2O*1^2)</td>
<td>0.21</td>
<td>&gt;0.21</td>
<td></td>
</tr>
</tbody>
</table>

### MUSCLE FORCES

<table>
<thead>
<tr>
<th></th>
<th>Actual</th>
<th>Pred</th>
<th>%Pred</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pmax (cmH2O)</td>
<td>121</td>
<td>138+/-39</td>
<td></td>
</tr>
<tr>
<td>Pimax (cmH2O)</td>
<td>-80</td>
<td>-91+/-25</td>
<td></td>
</tr>
</tbody>
</table>

DLCO 36\%
DL/VA 97\%
Mechanisms of Impairment in OHS

- Increased work of breathing
- Decreased mechanical efficiency of ventilation
- Heart failure
- Atelectasis with VQ mismatch

\[ \text{PaCO}_2 = \kappa \times \left( \frac{\text{VCO}_2}{\text{VA}} \right) \]

- OSA
Baseline PSG (9/2011)

- AHI 7.2 events/hr (NREM 2.2, REM 51)
- Nadir O2: 71%
- 49 minutes with sat <88%

Interpretation: This baseline polysomnogram with ETCO2 (end tidal CO2) monitoring shows obstructive sleep apnea worse in REM sleep. The study initially was done without oxygen supplementation and patient's baseline oxygen saturations were noted to be in mid-low 80's (with a nadir of 79%). Supplemental oxygen was added at 0.5 LPM and oxygen saturations were much improved and generally stayed above 90%. ETCO2 values ranged 52-54 mm.Hg, respiratory rate 22-24 breaths/minute during quiet wakefulness and were between 53-56 mm.Hg and respiratory rate of 18-20 breaths/minute during sleep. Periodic leg movements during wakefulness were noted.
OHS Case

- Treated with diuresis and BPAP 18/8 with 4L O2 in CCMU with improvement in pCO2 to low 60s.
- Ultimately discharged home on BPAP 18/8.
- Has had 2 f/u titrations in interim, most recent recommendation is BPAP 25/20 with 1L O2, but only observed in REM for 3 min.
- Most recent ABG: 7.36/48/68 on RA; HCO$_3^-$: 28
References

• The AASM Manual for the Scoring of Sleep and Associated Events, Version 2.0.
• The AASM International Classification of Sleep Disorders, Third Edition.