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NIPPV FOR THE HYPERCAPNIC COPD AND OBESITY HYPOVENTILATION SYNDROME PATIENT

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Disclosures

- No conflicts of interest
Learning Objectives

1. Recognize when to consider NIPPV over CPAP for hypercapnic COPD and obesity hypoventilation syndrome
2. Identify the appropriate NIPPV modality and settings to select for hypercapnic COPD and obesity hypoventilation syndrome
3. Understand the health outcomes associated with NIPPV use among patients with hypercapnic COPD and obesity hypoventilation syndrome

Outline

- Relevant pathophysiology
- Rationale and mechanism of NIPPV
- Clinical evidence supporting use of NIPPV
- Patient selection for NIPPV
- NIPPV initiation and titration
- Qualification criteria for NIPPV
Review Question: COPD

1. Which non-invasive ventilation modality has been demonstrated to prolong the time to hospital readmission or death in patients with hypercapnic COPD?
   A) Bilevel
   B) Bilevel-S/T
   C) Volume Assured Pressure Support
   D) Adaptive Servo Ventilation

Review Question: OHS

2. What clinical outcome has demonstrated improvement with bilevel compared to continuous positive airway pressure in patients with obesity hypoventilation syndrome?
   A) Daytime hypercapnia
   B) Quality of life
   C) Daytime sleepiness
   D) Pulmonary hypertension
Hypercapnic COPD: Definitions

- GOLD definition of COPD: post-bronchodilator \( \text{FEV}_1/\text{FVC} < 70\% \)
- Hypercapnia: \( \text{PaCO}_2 > 45 \text{ mmHg} \)

Hypercapnic COPD: Pathophysiology

- Lung parenchyma and airway destruction
  - Poor matching of ventilation to perfusion (i.e., V/Q mismatch or dead space ventilation)
- Imbalance between inspiratory muscle capacity and load placed on respiratory system
  - Hyperinflation changes configuration of diaphragm and shortens inspiratory muscles (mechanical disadvantage, atrophy, respiratory muscle weakness)
  - Excessive resistive load on respiratory muscles due to increased airway resistance and intrinsic positive end-expiratory pressure (iPEEP), inspiratory threshold
NIPPV Rationale/Mechanism in COPD

- Relief of ventilatory muscle fatigue
- Reduction in respiratory load
  - Decrease in lung hyperinflation with improvement in lung volumes
  - Decrease in iPEEP
- Augment alveolar ventilation
- Correcting CO₂ responsiveness (i.e., change in central chemosensitivity)
- Treating sleep-disordered breathing
- Benefits: improvements in dyspnea, nocturnal and daytime respiratory function, gas exchange, sleep quality, and functional status

Effective NIPPV Reduces PaCO₂

Factors that augment reduction in PaCO₂

- Higher IPAP
- Better adherence
- Higher baseline PaCO₂
NIPPV Improves Mortality/Readmission

- Baseline PaCO$_2$ $\geq$ 53 mmHg (mean 59.0 mmHg)
- Persistent hypercapnia after acute COPD exacerbation (2-4 weeks after resolution of respiratory acidemia)
- NIPPV targeted to reduce PaCO$_2$ by 3.75 - 7.5 mmHg overnight
- Mean IPAP 24 cmH$_2$O, EPAP 4 cmH$_2$O, backup rate 14 breaths/min
- Mean time to readmission or death 4.3 months in NIPPV group vs 1.4 months in control group

Hazard ratio 0.24 (0.11 - 0.49)

- Baseline PaCO$_2$ $\geq$ 51.9 mmHg (mean 58.5 mmHg)
- No exacerbation within 4 weeks
- NIPPV targeted to reduce PaCO$_2$ by at least 20% or < 48 mmHg
- Mean IPAP 21.6 cmH$_2$O, EPAP 4.8 cmH$_2$O, backup rate 16.1 breaths/min
- 1-year mortality 12% in NIPPV group vs 33% in control group

Murphy et al. JAMA. 2017;317:2177-2186

Overview of Randomized Controlled Trials

- PaCO$_2$ -7%, but not "stable" hypercapnic COPD
- 6MWD and FEV1
- PaCO$_2$ +5%
- PaCO$_2$ -10%
- PaCO$_2$ -7.4%
- PaCO$_2$ -6%
- 2 year follow-up

*Baseline PaCO$_2$ $\geq$ 54 mmHg

n = 101 102 57

N < 50 in NIPPV group
Duiverman. ERJ Open Res. 2018;4
Reasons for Heterogeneity

- Underpowered studies
- Patient selection and poorly characterized patient populations
  - Severity of COPD and degree of baseline hypercapnia
- NIPPV pressures capable of achieving adequate ventilation and reduction in PaCO$_2$
- Adherence with NIPPV therapy
- Duration of therapy and follow-up
- Underlying OSA

The Overlap Syndrome

Adjust for age, sex, BMI, smoking, EtOH, comorbidities, COPD severity, AHI, daytime sleepiness

PaCO$_2$ ≥ 45 mmHg (average 51.6 mmHg)
Selecting COPD Patients for NIPPV

- Patients most likely to derive a benefit are those with most severe and advanced disease
- Daytime PaCO$_2$ $\geq$ 52 mmHg and O$_2$ desaturation during sleep (i.e., SpO$_2$ $\leq$ 88% for $\geq$ 5 minutes) despite use of supplemental O$_2$ at $\geq$ 2 L/min
- History of hospitalization for acute respiratory failure with persistent, severe hypercapnia
- Others recovering from acute exacerbation that necessitated use of continuous NIPPV during hospitalization

Initiation of NIPPV for COPD

- Optimal approach has not been determined
- Typically start bilevel with EPAP of 5 cmH$_2$O and IPAP of 10 cmH$_2$O and gradually increase
  - Final IPAP near 15 cmH$_2$O (range 12-20 cmH$_2$O)
    - Adjust IPAP for pressure support (PS) that achieves goal tidal volume (~8 ml/kg ideal body weight), as tolerated
  - Final EPAP at least 5 cmH$_2$O below IPAP
    - Adjust EPAP to eliminate obstructive apneas
    - If ineffective trigger, adjust EPAP to overcome high iPEEP
“High Intensity” NIPPV

- Specific NIPPV settings to achieve normocapnia or lowest PaCO\(_2\) levels possible
- Often requires high IPAP ± backup rate

**AVAPS/iVAPS**
- Volume-assured pressure support
  - No proven clinical benefit of switching from high intensity NIPPV; possible physiological advantages in breathing pattern

**AVAPS AE**
- Includes auto-titrating EPAP
  - Optimize EPAP to maintain airway patency

**Mouth Piece Ventilation (MPV)**
- Prevents deterioration of gas exchange as well as NIPPV in COPD exacerbations with mild to moderate acidosis, and it is better tolerated
- Ventilation before oxygenation
Challenges

- Patient comfort and tolerance of high pressures
  - Concern for hyperinflation with high backup rate
  - Important to titrate stepwise (usually over several days)
- Cardiovascular side effects
  - High IPAP may reduce cardiac output in patients with cardiac failure
- Initiation of NIPPV in the hospital or ventilator facility
  - Not mandatory for success
  - Reimbursement for devices with backup rate
  - Standard bilevel devices only allow for PS of 10 cmH₂O

Qualifying for NIPPV: COPD

ABG with PaCO₂ ≥ 52 mmHg (awake and on prescribed FiO₂) AND Sleep oximetry with oxygen saturation ≤ 88% for ≥ 5 cumulative minutes on ≥ 2 L/min O₂ or prescribed FiO₂ (whichever is higher) AND OSA and CPAP treatment have been considered and ruled out (formal sleep testing not required)

E₄₇₀ = Bilevel S

Conversion from S to ST

Situation 1 (after period of initial use of E₀₄₇₀):
ABG with PaCO₂ worsening ≥ 7 mmHg vs original ABG (awake and on prescribed FiO₂) AND Facility-based PSG on E₄₇₀ with oxygen saturation ≤ 88% for ≥ 5 cumulative minutes (not caused by OSA – AHI < 5)

E₄₇₁ = Bilevel ST

Situation 2 (no sooner than 61 days after initial use of E₀₄₇₀):
ABG with PaCO₂ ≥ 52 mmHg (awake and on prescribed FiO₂) AND Sleep oximetry on E₄₇₀ with oxygen saturation ≤ 88% for ≥ 5 cumulative minutes on ≥ 2 L/min O₂ or prescribed FiO₂ (whichever is higher)
OHS: Definition and Consequences

- OHS definition: awake alveolar hypoventilation (PaCO₂ > 45 mmHg) in obese (BMI > 30 mg/kg²) patients which cannot be attributed to other causes (i.e., neuromuscular, metabolic, lung, or chest wall diseases)
- OHS will progress if not treated with PAP, and it is associated with significantly worse cardiovascular morbidity, mortality, and healthcare utilization vs eucapnic OSA and eucapnic obese patients
- Can lead to pulmonary hypertension, right heart failure, and increased risk of hospitalization due to acute-on-chronic hypercapnic respiratory failure

OHS: Pathophysiology

NIPPV Rationale/Mechanism in OHS

- Controversy remains as to the preferred modality of positive airway therapy
- Conceptually, NIPPV should be more effective than CPAP, as it addresses the various complex pathophysiological disturbances that result in OHS:
  - EPAP for upper airway resistance, chest wall and abdominal resistance, and atelectasis
  - IPAP for altered ventilatory drive, worsened hypoventilation during sleep, and rest of respiratory muscles

Pickwick Study

- RCT comparing NIPPV, CPAP, and lifestyle modification in OHS patients with severe OSA
- Main outcome: daytime PaCO₂
- Total n = 221, follow-up = 2 months
- Greatest reduction in PaCO₂ and bicarbonate in NIPPV group, but not significant vs CPAP
- FEV₁ and 6MWD improved more with NIPPV than CPAP

Masa et al. Am J Respir Crit Care Med. 2015;192:86-95
Pickwick Study: Update

- RCT of CPAP vs NIPPV for OHS with severe OSA
- Primary outcome: hospitalization days
- Secondary outcomes: hospital resource utilization, mortality, cardiovascular events, compliance, side effects
- Total n = 215
- Median follow-up = 5.42 years
- Hospital days/yr was 2.19 ± 5.65 for CPAP and 1.44 ± 3.07 for NIV (adjusted P = 0.12)
- No difference in secondary outcomes

Quiroga et al. European Respiratory Journal 2018; 52: Suppl. 62, OA5414

Cardiovascular Effects of NIPPV

- Secondary analysis of Pickwick Study
- Conventional transthoracic 2D and doppler echo performed at baseline and after 2 months
- At baseline 55% of patients had pulmonary hypertension (PH), 51% with left ventricular hypertrophy (LVH)
- NIPPV lowered systolic pulmonary artery pressure, but CPAP did not (−3.4 mmHg, −5.3 to −1.5; adjusted P = 0.025 vs control and P = 0.033 vs CPAP)
  - Greater reduction with NIPPV in those with PH at baseline (−6.4 mm Hg, −9 to −3.8)
- NIPPV reduced left ventricular mass and improved 6MWD (32 m; 19 to 46)

Corral et al. Thorax. 2018;73:360-368
Selecting OHS Patients for NIPPV

- ~90% of patients with OHS have coexisting OSA → CPAP is appropriate initial modality
- Bilevel is appropriate for patients with OHS and sleep-related hypoventilation (i.e., few obstructive events during sleep)
  - Patients with OHS and OSA who fail or do not tolerate CPAP should be treated with bilevel
  - Patients who fail or do not tolerate bilevel should be treated with average volume-assured pressure support
- Features that suggest bilevel may be more appropriate than CPAP:
  - Lower AHI on PSG
  - More restrictive physiology on PFTs
  - More severe and persistent O₂ desaturation during PSG

Initiation of NIPPV for OHS

- At a minimum, set EPAP at 4 cmH₂O and IPAP at 8 cmH₂O
- EPAP should be adjusted for obstructive apneas
  - Some studies have adjusted EPAP for all obstructive events (obstructive apneas, hypopneas, flow limitation, and snoring) → results in higher EPAP
  - Increase IPAP simultaneously to maintain pressure difference between EPAP and IPAP
- IPAP should be adjusted for hypoventilation (which may be manifested by persistent O₂ desaturation unrelated to obstructive events) and hypopneas
Monitoring/Goals of NIPPV in OHS
• Normalize PaCO₂ (< 45 mmHg) during wakefulness and sleep
• Eliminate O₂ desaturation during wakefulness and sleep
• Treat sleep disordered breathing (obstructive apneas, hypopneas, and hypoventilation)
• Improve sleep architecture and quality
• Relieve symptoms (daytime hypersomnolence, morning headache)
• Prevent complications (erythrocytosis, pulmonary hypertension, right heart failure, mortality)

NIPPV Improvement in SpO₂ During Sleep Correlates with Reduction in Bicarbonate
• Total n = 35
• 1-month follow-up
• Mean IPAP 18 cmH₂O, EPAP 11 cmH₂O, backup rate 13 breaths/min

Other NIPPV Options for OHS

- AVAPS/iVAPS
  - Residual airway obstruction on bilevel (but EPAP fixed)
  - Sufficient alveolar ventilation cannot be achieved with bilevel (due to decreased respiratory system compliance)
  - Can achieve higher PS vs bilevel (which has maximum of 10 cmH₂O) and higher overall pressure (30 vs 25 cmH₂O)
  - Similar improvement in daytime PaCO₂ as bilevel
- AVAPS AE
  - Likely better for obstructive events and maintaining airway patency
  - Can achieve even higher maximal pressures (i.e., 50 cmH₂O)

Qualifying for NIPPV: OHS

ABG with PaCO₂ ≥ 45 mmHg (awake and on prescribed FiO₂) AND Spirometry with FEV₁/FVC ≥ 70% AND ABG with PaCO₂ worsening ≥ 7 mmHg vs original ABG (done during sleep or immediately upon awakening on prescribed FiO₂)

PSG or HST with oxygen saturation ≤ 88% for ≥ 5 minutes (not caused by OSA – AHI < 5)

Conversion from S to ST

Covered E0470 is being used AND Spirometry with FEV₁/FVC ≥ 70% AND ABG with PaCO₂ worsening ≥ 7 mmHg vs ABG used to qualify for E0470 (done during sleep or immediately upon awakening on prescribed FiO₂)

PSG or HST on E0470 with oxygen saturation ≤ 88% for ≥ 5 minutes (not caused by OSA – AHI < 5)

E470 = Bilevel S
E471 = Bilevel ST
Key Points

- NIPPV addresses the underlying pathophysiology of hypercapnic COPD and OHS, manifest as reduction in PaCO₂
- High intensity NIPPV has demonstrated physiological and clinical benefit in hypercapnic COPD (reduction in mortality and readmissions)
- NIPPV improves lung function, exercise capacity, pulmonary hypertension, and left ventricular hypertrophy vs CPAP in OHS patients
- Appropriate patient selection for NIPPV is essential
References


Thank You!

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