به نام خداوند جان و خرد

NIV in Obesity Hypoventilation Syndrome

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Obesity hypoventilation syndrome (OHS)

INTRODUCTION

Obesity hypoventilation syndrome (OHS) is diagnosed in patients with obesity (ie, body mass index [BMI] >30 kg/m) when awake alveolar hypoventilation (partial pressure of arterial carbon dioxide >45 mmHg) cannot be attributed to other causes (eg, neuromuscular diseases, COPD, kyphoscoliosis).

OHS is associated with increased cardiovascular morbidity and mortality.

Consequently, early detection and treatment are crucial to minimize these adverse effects.

Staging OHS

Patients with obstructive sleep apnea (OSA) and no hypercapnia were considered stage 0.

Stages I and II represented patients with obesity-associated sleep hypoventilation but normal awake arterial pressure of carbon dioxide and either serum bicarbonate <27 mmol/L (stage I) or >27 mmol/L (stage II).

Stages III and IV encompassed classically defined OHS patients with or without concurrent OSA.

Those in stage IV were distinguished from stage III by the presence of significant cardiometabolic comorbidities.

Alveolar hypoventilation in patients with obesity occurs when the normal compensatory ventilatory mechanisms that maintain adequate ventilation fail.

OHS is likely due to a complex interaction of several physiologic abnormalities, including:

sleep disordered breathing (obstructive sleep apnea and/or sleep hypoventilation),

altered pulmonary mechanics (restriction, ventilation/perfusion mismatching, reduced respiratory muscle strength),

altered ventilatory control (reduced neural drive and ventilatory responsiveness, leptin resistance),

and increased carbon dioxide production

OHS Prevalence

Obese population – The prevalence of OHS increases as body mass index (BMI) rises:

In several retrospective studies among patients with OSA, the prevalence of OHS

in those with a BMI of 30 to 35 kg/m is 8 to 12 percent, higher among those with a BMI ≥40 kg/m (18 to 31 percent) and those with a BMI ≥50 kg/m (50 percent).

General population – Estimates based on rates of obesity and obstructive sleep apnea

(OSA) in the community suggest 0.15 to 0.3 percent of the adult population in the

United States are likely to have OHS

Obesity hypoventilation syndrome (OHS)

Noninvasive positive airway pressure (PAP) and weight loss are first-line treatment for patients with OHS, although the effect on survival is unclear.

For patients with OHS, we recommend noninvasive positive airway pressure (PAP) therapy during sleep rather than lifestyle modifications alone in order to improve symptoms and parameters of awake ventilation (ie, arterial partial pressure of carbon dioxide [PaCO2]).

Mode selection for initial PAP therapy is determined by the presence or absence of comorbid obstructive sleep apnea (OSA) based on the results of in-laboratory polysomnography (PSG).

Approximately 90 percent of patients with OHS have coexisting obstructive sleep apnea (OSA), in which case continuous positive airway pressure (CPAP) is the initial mode of Choice.

For patients with OHS and sleep-related hypoventilation (ie, few obstructive events during sleep), and patients with acutely decompensated OHS, bilevel positive airway pressure (BPAP) is usually the initial mode of choice.

Patients with OHS and OSA who fail or do not tolerate CPAP are also treated with BPAP.

For those who fail or do not tolerate BPAP, a hybrid mode (average volume-assured pressure support) or, less commonly, volume-cycled ventilation may be chosen.

While PAP is mostly administered during sleep, similar principles apply when PAP is administered during wakefulness when patients present with acute decompensation of OHS.

- Continuous positive airway pressure ventilation (CPAP) during sleep is the first line mode used in this population. CPAP delivers a constant pressure throughout the respiratory cycle.
- In OSA, the main effect of CPAP is the maintenance of upper airway patency, thereby preventing obstructive and hypopneic events and allowing oxygenation and ventilation to continue throughout the respiratory cycle.
- In patients with OHS and OSA, initial settings for fixed CPAP during sleep are similar to those in patients with OSA without coexisting OHS. Typically, titration is performed in a laboratory setting with polysomnographic monitoring.
- Auto-adjusting CPAP should not be used, as the limited information available on its use suggests that it improves hypercapnia in only half of in patients with OHS.

Data report reduction of sleep-related and awake arterial carbon dioxide tension ($PaCO_2$) as well as quality of life improvements after the initiation of CPAP, although normalization of $PaCO_2$ is not universal .

Since CPAP does not directly augment ventilation other than by maintaining upper airway patency, the CPAP-related improvement of hypercapnia during both wakefulness and sleep may be due to relief of respiratory muscle fatigue and/or augmentation of central ventilatory drive .

Similarly, CPAP may not universally eliminate nocturnal oxyhemoglobin desaturation, which is a signal of persistent nocturnal hypoventilation.

One study reported that forty-three percent of the patients with OHS plus OSA continued to spend more than 20 percent of their total sleep time with a peripheral oxygen saturation (SpO_2) <90 percent despite adequate treatment of OSA with CPAP.

- Best illustrating this is a randomized trial of 215 patients that reported that among patients with OHS and OSA (apnea hypopnea index >30 events per hour), BPAP and CPAP resulted in a similar number of hospitalization days over a five-year period.
- In addition, no difference was seen in other outcomes including weight loss, lung function, arterial blood gas (ABG) improvement, need for supplemental oxygen, and health-related quality of life.
- Subsequent subgroup analysis of the two treatment groups based upon the pretreatment level of PaCO2 (45 to 49.9 or >50 mmHg) demonstrated no difference in subsequent awake PaCO2 or PaO2 over three years of follow-up between those patients treated with CPAP or BPAP .
- suggesting that the degree of hypercapnia at baseline should not be the sole reason to choose BPAP over CPAP

- **Predictors of a response to CPAP** in patients with OHS are unclear patients.
- who benefit from nocturnal CPAP therapy tend to have a higher baseline apnea hypopnea index (AHI), less restrictive physiology on spirometry, and less severe oxyhemoglobin desaturation during baseline polysomnography than patients who do not improve with CPAP.
- However, these features are not specific and should not determinate the clinician from initially choosing CPAP in this population.
- Noninvasive positive airway pressure (PAP) therapy is generally provided in conjunction with other therapies for OHS, including weight loss and supportive therapies (eg, avoidance of alcohol and sedatives).
- **The goals of treatment:**
- Normalization of the arterial carbon dioxide tension (PaCO2) during wakefulness and sleep (ie, PaCO2 <45 mmHg)
- Elimination of oxyhemoglobin desaturation during wakefulness and sleep,
- Relief of the symptoms of OHS (typically daytime hypersomnolence),
- Prevention of complications including erythrocytosis, pulmonary hypertension, and, right heart failure, Treatment of underlying OSA (ie, elimination of obstructive and hypopnea events) and/ or sleep-related hypoventilation (ie, nonobstructive events) , Improvement of sleep architecture and quality of life.

- **Assess symptoms** — Within one month of therapy, patients who are prescribed noninvasive PAP should be assessed for their adherence to PAP therapy and for symptoms and signs of persistent sleep-related hypoventilation,
- **Assess indicators of alveolar hypoventilation** —
- ABG analysis is the gold standard method of assessing alveolar ventilation. However, overnight ABG analysis requires placement of an indwelling arterial catheter or multiple arterial blood draws, both of which are impractical in most sleep laboratories.
- Awake ABG – Periodic (eg, within one to three months) awake ABGs are useful early after PAP titration to verify that alveolar hypoventilation has improved.
- One retrospective cohort study of 75 treated OHS patients (mostly with CPAP) reported correlations between the hours of daily use and the reduction in daytime $PaCO_2$ and the increase in PaO_2 .
- Residual oxyhemoglobin desaturation during sleep on PAP therapy typically necessitates polysomnography to assess for residual obstructive events or persistent nocturnal hypoventilation.

- **Indication for repeat in laboratory polysomnography:**
- Clinical manifestations of persistent alveolar hypoventilation (eg, nocturnal dyspnea, a sensation of smothering at night, chronic morning headaches, failure of awake blood gases to improve) despite documented adherence with noninvasive PAP.
- Persistent alveolar hypoventilation suggests that the type or level of PAP may need to be changed.
- **Second line therapies** — Patients with OHS who fail or do not tolerate continuous positive airway pressure (CPAP) should be treated with bilevel positive airway pressure (BPAP).
- Patients in this category include those who, despite adherence to adequate CPAP therapy, fail to normalize daytime partial arterial pressure of carbon dioxide (PaCO 2; assuming hypercapnia is OHS-related), have oxyhemoglobin desaturation to <88 percent that is suggestive of residual hypoventilation, or are intolerant of CPAP despite troubleshooting maneuvers.
- When CPAP is applied during polysomnography, changing to BPAP should be considered when, despite relief of obstructive apneic and hypopneic events, residual oxyhemoglobin desaturation (SaO2 remains <88 percent) suggests persistent hypoventilation that requires additional inspiratory pressure support.

Bilevel positive airway pressure

- **Initial settings** — During BPAP therapy, an inspiratory positive airway pressure (IPAP) and an expiratory positive airway pressure (EPAP) are independently titrated and set.
- EPAP is adjusted to overcome upper airway occlusion, and IPAP is increased to augment ventilation further.
- Tidal volume correlates with the. difference between the IPAP and the EPAP.
- As an example, tidal volume is greater using an IPAP of 15 cm H2 O and an EPAP of 5 cm H2O (difference or "delta" of 10 cm H O), than an IPAP of 10 cm H O and an EPAP of 5 cm H2 O (difference or "delta" of 5 cm2 H O).
- Alveolar ventilation is enhanced by a larger tidal volume, assuming that the respiratory rate is constant.
- In cases where OHS and OSA has not been treated with CPAP, initial IPAP and EPAP are usually started at 8 and 4 cm H 2O, respectively and incrementally increased until airway obstruction is resolved and hypoventilation is eliminated (maximum IPAP is typically 20 to 30 cm H2 O for adults).
- A backup respiratory rate (ie, spontaneous/timed mode) set below the baseline sleep-related respiratory rate is usually provided to augment spontaneous respiratory efforts should central apneas or a low respiratory rate complicate BPAP therapy.
- However, judicious use of this mode is necessary to prevent patient/ventilator asynchrony or periodic breathing, which may result in sleep fragmentation that limits improvement of OHS related hypersomnia

- A meta-analysis of seven studies also confirmed that BPAP, when compared with lifestyle counselling, was superior in improving the PaCO2 (-2.9 mmHg; 95% CI -4.28 to -1.52 mmHg), PaO2 (2.89 mmHg, 95% CI 0.33 to 5.6 mmHg), and bicarbonate level (-2.55 mmol/L, 95% CI -3.28 to -0.88 mmol/L).
- An impact on mortality is less certain.
- **Several advantages BPAP compared with CPAP including:**
- Active ventilation (provides inspiratory pressure support)
- A lower mean airway pressure when treating OSA, which may lead to better tolerance of the therapy
- Better respiratory muscle rest
- More rapid improvement of respiratory acidosis
- Compensation for minor air leaks

- **Disadvantages BPAP compared with CPAP include:**
- Potential for patient-ventilator asynchrony and associated ineffective ventilation.
- Ineffective triggering due to the failure of the BPAP device to detect inspiratory efforts is generally managed by raising EPAP to ensure airway patency.
- Potential for persistent hypoventilation due to development of central apneas, ineffective triggering of IPAP, or tidal volume limitation due to severe residual upper airway obstruction (ie, obstructive apneas/hypopneas) or decreased respiratory system Compliance.
- To address the problem of central apnea development, many experts use BPAP ST in a spontaneous/timed (S/T) mode with a backup rate.
- BPAP devices are more expensive

Average volume-assured pressure support:

- (AVAPS) is a hybrid mode of PAP with features of standard BPAP and volume-cycled positive pressure ventilation (VCPPV).
- In the AVAPS mode, the IPAP varies between respiratory cycles in order to achieve a preset tidal volume, which is usually set at 7 to 10 mL per kg of ideal body weight.
- AVAPS is an option in patients with OHS who fail or cannot tolerate continuous or bilevel positive airway pressure (CPAP, BPAP, respectively) despite optimal settings and adherence.
- Patients who fail may include those with residual upper airway obstruction or a reduction in respiratory system compliance which is so severe that sufficient alveolar ventilation cannot be achieved with CPAP or BPAP despite optimization of settings (eg, increasing inspiratory positive airway pressure [IPAP] or increasing the differential between IPAP and expiratory PAP [EPAP]).

Volume-cycled ventilation

- Volume-cycled positive pressure ventilation (VCPPV) is reserved for situations when sufficient alveolar ventilation cannot be achieved with BPAP.
- VCPPV delivers a set tidal volume.
- VCPPV ensures adequate ventilation by generating pressures high enough to overcome the physiologic limitations (upper airway obstruction and reduced respiratory compliance) presented by the patient with OHS.
- This mode may be tried when BPAP fails in a patient with acute decompensation of OHS.
- Short-term VCPPV during sleep has been reported to improve daytime hypercapnia, with many patients eventually able to return to long-term CPAP or BPAP therapy.

- A small minority (about 10 percent) of patients with OHS have sleep-related hypoventilation (few obstructive events) for which bilevel positive airway pressure (BPAP) is typically the first treatment of choice.
- An alternative is volume-targeted pressure support ventilation.
- Continuous positive airway pressure (CPAP) is not effective in these patients since this form of sleep disordered breathing is not associated with obstructive events
- **Bilevel positive airway pressure** — BPAP initiation is similar to that in patients with obstructive sleep apnea (OSA) who have not been previously titrated on PAP. However, it is critical that a backup respiratory rate be set using the spontaneous/timed mode(BPAP- ST) in this population.
- The patients with BPAP therapy with higher adherence (>4 hours of use per day)have beneficial outcomes related to hospital admissions, emergency department visits, and mortality.

PATIENTS WITH ACUTE HYPERCAPNIC RESPIRATORY FAILURE AND OHS

- Patients who present with an acute decompensation of OHS (ie, acute on chronic hypercapnic respiratory failure) should have noninvasive positive airway pressure (PAP) ventilation initiated expeditiously in a monitored inpatient setting, assuming that they are acceptable candidates for this therapy (eg, able to cooperate, can protect their own airway, are hemodynamically stable.
- In this setting, timely institution of noninvasive ventilation (NIV) successfully averts endotracheal intubation in over 90 percent of patients..
- Patients who are not candidates for NIV or who fail this therapy should be considered for urgent endotracheal intubation with mechanical ventilation.

- Bilevel positive airway pressure (BPAP) is the mode that is generally tried first, with volume cycled positive pressure ventilation (VCPPV) reserved for situations when sufficient alveolar ventilation cannot be achieved with BPAP.
- Continuous positive airway pressure (CPAP) should **not** be used in this setting.
- In cases where the diagnosis of OHS is presumed and the patient has not received PAP therapy in the chronic setting, these modes are used until the patient is sufficiently stable to undergo polysomnography with formal titration of PAP settings (ideally within the next two to three months).
- In those already receiving CPAP, switching to BPAP is appropriate and in those already on BPAP, inspiratory PAP (IPAP) may be cautiously increased above its chronic setting with most patients eventually able to return to long-term CPAP or BPAP therapy.

- All patients hospitalized with acute decompensation of OHS should be discharged home on PAP.
- A systematic review of hospitalized patients with decompensated OHS demonstrated that in-hospital application of empiric PAP (over 90 percent NIV) and discharging patients home on this therapy markedly reduced three-month mortality (relative risk 0.12) when compared with those patients discharged without PAP.

- If PAP naïve, we typically begin with inspiratory positive airway pressure (IPAP) and expiratory positive airway pressure (EPAP) settings of 4 cm H 2O and then increase the IPAP every several minutes in increments of 2 cm H 2O until the patient appears more comfortable and there is an acceptable respiratory rate (eg, <30 breaths per minute), oxyhemoglobin saturation (eg, ≥90 percent), heart rate (eg, ≤100 beats per minute), and degree of ventilation (eg, pH >7.3 on serial arterial blood gases 1 to 2 hours later).

- VCPPV, the ventilator mode, respiratory rate, tidal volume, inspired oxygen concentration, and positive end-expiratory pressure (PEEP) must be selected (similarly to invasive mechanical ventilator settings).
- The largest tidal volume that consistently maintains an airway pressure less than 30 cm H2 O is generally chosen (generally 7 to 10 mL/Kg of ideal body weight), and the respiratory rate is then set to achieve a minute ventilation of 6 to 10 L/min.
- The inspired oxygen concentration should be titrated to maintain adequate oxyhemoglobin saturation (eg, ≥90 percent).
- Failure of oxygenation to improve quickly may require further increases in EPAP.
- IPAP is generally increased simultaneously in order to maintain a pressure difference between EPAP and IPAP that is sufficient to decrease work of breathing and adequately ventilate the patient.
- **Invasive mechanical ventilation** — Patients who are not candidates for noninvasive ventilation or who fail this therapy should be considered for urgent endotracheal intubation with mechanical ventilation

SUPPLEMENTAL OXYGEN DURING POSITIVE AIRWAY PRESSURE VENTILATION

- Hypoxemia (sleep-related and awake) is common in patients with OHS, especially in those with coexisting obstructive sleep apnea (OSA).
- Supplemental oxygen should only be administered when positive pressure therapy alone is insufficient to eliminate hypoxemia.
- Supplemental oxygen during sleep is titrated during polysomnography to eliminate hypoxemia or severe oxyhemoglobin desaturation after the optimal settings of positive pressure therapy have been established. Supplemental oxygen while awake can be titrated using oximetry at rest and with exertion.
- It should be titrated to the lowest flow that maintains a oxyhemoglobin saturation of >90 percent. Occasionally for intractable hypoxemia, a nasal cannula can be placed underneath the mask.
- The need for supplemental oxygen frequently decreases as the patient's cardiopulmonary status improves with nocturnal PAP therapy.
- Supplemental oxygen **alone** (without positive pressure therapy) is **inadequate** therapy for OHS.
- Although it may improve nocturnal oxyhemoglobin desaturation, it does not relieve upper airway obstruction or augment ventilation, and it may acutely worsen carbon dioxide retention even in stable patients with OHS.

Advantages and disadvantages of the different methods for administering positive airway pressure

Mode of positive pressure ventilation	Advantages	Disadvantages
CPAP	Inexpensive	Lack of inspiratory pressure support
	Widely available	
Bi-level	Widely available	Tidal volume may be limited by patient-related factors
	Can provide inspiratory pressure support to augment tidal volume	
	Leak tolerant	
Volume-cycled	Can set specific respiratory parameters	More expensive
		Less widely available
		Less well tolerated than pressure support devices
		Leaks lead to loss of tidal volume

Potential indicators of success in noninvasive ventilation

Younger age
Lower acuity of illness (APACHE score)
Able to cooperate, better neurologic score
Less air leaking, intact dentition
Moderate hypercarbia ($PaCO_2$ >45 mmHG, <92 mmHG)
Moderate acidemia (pH <7.35, >7.10)
Improvements in gas exchange as well as heart and respiratory rates within first 2 hours

- Weight loss
- avoidance of alcohol and sedatives
- Progestin
- Acetazolamide
- Tracheostomy


Thanks for attention