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Editorial

Challenges in the Treatment of Obesity Hypoventilation Syndrome With Persistent Nocturnal Hypoxemia: CPAP vs. NIV

Desafío en el tratamiento del síndrome de hipoventilación obesidad con hipoxemia nocturna persistente: CPAP vs. VMNI

In patients with obesity hypoventilation syndrome (OHS) and severe obstructive sleep apnea (OSA), continuous positive airway pressure (CPAP) is the recommended first-line treatment.[1,2] However, there is controversy regarding the most appropriate therapeutic strategy for patients with persistent nocturnal hypoxemia despite adequate control of obstructive events with CPAP. Specifically, whether to continue CPAP therapy with the addition of supplemental oxygen or switch to non-invasive ventilation (NIV) remains a subject of debate.[1]

First, nocturnal hypoventilation despite CPAP treatment must be ruled out in OHS patients, as its confirmation necessitates switching to NIV.[1,2] The gold standard for detecting nocturnal hypoventilation is nocturnal transcutaneous capnography, which confirms hypoventilation when the transcutaneous CO_2 pressure ($PtCO_2$) increases to ≥55 mmHg for ≥10 min, or rises by ≥10 mmHg above baseline and exceeds 50 mmHg for ≥10 min.[3] In the absence of capnography, a serum bicarbonate level <27 mmol/L has a high negative predictive value.[1] Additionally, morning arterial blood gas analysis and overnight pulse oximetry may aid diagnosis, although normal results do not exclude nocturnal hypoventilation. Georges et al.[4] identified hypoventilation in 30% of OHS patients without morning hypercapnia or nocturnal desaturation, and suggested that CPAP may maintain adequate SpO_2 by increasing functional residual capacity despite ongoing hypoventilation.

When nocturnal hypoxemia persists in the absence of hypoventilation and despite optimized CPAP, employing CPAP with supplemental oxygen or the initiation of NIV may be considered.[1] However, no validated threshold exists to define clinically significant hypoxemia in OHS.[1] Traditionally, a T90 >30% or SpO_2 <88–90% for ≥5 min is accepted,[5] although these definitions are derived from COPD studies and have not been specifically validated in OHS patients.

Currently, there are no specific studies that address the management of persistent hypoxemia in OHS. In the Pickwick clinical trial led by Masa et al.,[6] CPAP and NIV were compared as initial treatments for OHS patients with severe OSA, and no differences were found in mortality, cardiovascular events, or blood gas results after 36 months. A subsequent sub-analysis[7] reported a higher incidence of morning headache and confusion in patients treated with CPAP and supplemental oxygen compared to those treated with NIV, suggesting nocturnal hypoventilation in the former group and supporting a switch to NIV for patients requiring both CPAP and oxygen. Other studies have proposed that OHS patients with elevated T90 and no residual obstructive events on CPAP may benefit more from NIV.[8–10]

Identifying the predominant pathophysiological mechanism is essential for anticipating treatment response. The main contributing factors in OHS with severe OSA include: (1) upper airway collapsibility, (2) altered respiratory center response, and (3) thoracic changes secondary to obesity, such as basal atelectasis, increased intrinsic positive end-expiratory pressure (PEEP), respiratory muscle weakness with impaired diaphragmatic mobility, and reduced functional residual capacity and tidal volume. These alterations promote hypoxemia by disrupting the ventilation/perfusion ratio.[2]

Supporting the use of CPAP with supplemental oxygen is the improvement in T90, as persistent abnormal T90 has been associated with increased mortality, higher blood pressure levels, and elevated inflammatory markers, which can ultimately lead to a higher cardiovascular risk.[11–13] Moreover, this approach is more cost-effective than NIV.[6] However, this strategy is not without risk, as supplemental oxygen may elevate $PaCO_2$ via the inhibition of hypoxic vasoconstriction and the Haldane effect,[14] potentially increasing $PaCO_2$ by 2–4 mmHg or even causing respiratory acidosis in OHS patients.[15] Therefore, transcutaneous capnography is recommended to exclude hypoventilation during CPAP with supplemental oxygen.

From a pathophysiological perspective, CPAP corrects upper airway collapsibility and partially addresses thoracic alterations due to obesity. However, in patients with persistent hypoxemia, CPAP alone may be insufficient. In these cases, more pronounced mechanical abnormalities and greater parenchymal involvement – such as atelectasis, reduced lung volumes, or respiratory muscle weakness – may limit the effectiveness of CPAP, preventing adequate ventilatory compensation. Under these circumstances, NIV could represent a more effective therapeutic option with potential clinical benefits.[8].

NIV has several relevant physiological effects in OHS. It improves minute and alveolar ventilation, resulting in increased PaO_2 and reduced $PaCO_2$. The application of external PEEP promotes alve-

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olar recruitment and reduces intrinsic PEEP and atelectasis, thus improving the ventilation/perfusion ratio. NIV also increases tidal volume, thereby reducing the respiratory rate and allowing the respiratory muscles to rest. Additionally, it decreases the mechanical load on the ventilatory muscles, particularly the diaphragm, which in obese patients is both overloaded and functionally weakened. These effects, following the correction of hypoxemia, may help restore the responsiveness of the respiratory center.[16] However, despite these benefits, adverse effects may occur, including air leaks, patient-ventilator asynchrony, generation of intrinsic PEEP, and potential hemodynamic interactions. Furthermore, NIV is more expensive than CPAP.[6,16]

Currently, there are no standardized criteria or validated thresholds to guide the management of persistent hypoxemia in OHS. The decision between continuing CPAP with supplemental oxygen or initiating NIV must be individualized based on the predominant pathophysiological mechanism and observed clinical response. NIV may be particularly useful for patients with persistent hypoxemia not explained by obstructive events or other pathologies, as it simultaneously targets multiple contributing factors in OHS by providing inspiratory support and expiratory positive pressure.[2] Nevertheless, current evidence does not definitively establish which strategy provides greater clinical or prognostic benefit.

In conclusion, both CPAP with supplemental oxygen and NIV may be valid treatment options for OHS patients with residual hypoxemia, pending further scientific evidence to support a clear recommendation. Future studies are needed to define clinical thresholds, develop follow-up strategies, and compare the efficacy and cost-effectiveness of both approaches. Additionally, the identification of specific OHS phenotypes is essential to determine which patients may benefit most from each therapy, ultimately enabling individualized treatment strategies.

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Conflicts of interest

The results presented have not been previously published. The authors declare no competing interests.

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