Outcomes for Obese Patients with Chronic Respiratory Failure

Results from Observational and Randomized Controlled Trials

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KEYWORDS

• Continuous positive airway pressure • Noninvasive ventilation • Chronic respiratory failure • Obesity • Outcomes

KEY POINTS

- Observational cohort data support the clinical effectiveness of positive airway pressure (PAP) therapy in improving clinical outcome in obese patients with chronic respiratory failure.
- There are limited data to recommend a single PAP strategy, and a considered approach to the phenotype of sleep-disordered breathing must be applied.
- Phenotyping of sleep-disordered breathing resulting in obesity-related chronic respiratory failure is essential for interpreting the current published data and clinical decision making on which PAP strategy to employ.
- Reversal of chronic respiratory failure should be the long-term aim of PAP therapy.
- 4 hours per night use of PAP therapy should be targeted for treatment of obese patients with chronic respiratory failure.
- Physical activity should be augmented following initiation of PAP therapy to improve long-term obesity-related morbidity.

INTRODUCTION

Obesity hypoventilation syndrome (OHS) was originally reported by Auchincloss and colleagues[1] in 1955, with the term Pickwickian syndrome coined the following year.[2] Although the use of mechanical ventilatory support to manage the acute decompensated episodes was described some years later,[3] the first report of the use of positive airway pressure (PAP) to improve sleep-disordered breathing and reverse the associated daytime chronic respiratory failure as a clinical outcome was not reported until several decades later.[4] Despite the increasing global prevalence of this condition across Europe, North America, and Australasia, there are still few randomized controlled trials to support and direct clinical decision making. Currently, clinicians are required to

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develop their own clinical practice primarily based on limited physiologic and clinical data. This article will emphasize the important outcome parameter that the clinician needs to consider.

TARGET POPULATIONS AND THE PHENOTYPE OF PATIENTS WITH SLEEP-DISORDERED BREATHING

In the current definition of OHS, chronic respiratory failure as a consequence of sleep-disordered breathing is an essential component.[5] Although this is predominantly manifested as obstructive sleep apnea (OSA), lone hypoventilation can be the cause in around 10% of cases,[6] highlighting the complexities with physiologic phenotyping of sleep-disordered breathing in clinical practice. There is a requirement, when considering patient-centered, clinician-centered, and health care utilization outcomes, of reflecting on 3 patterns of sleep-disordered breathing that cause obesity-related chronic respiratory failure from severe OSA to a combination of OSA and OHS overlap and lone OHS. This will allow a comprehensive evaluation of the outcome data from the clinical trials, because although a trial may be reported as negative, the clinician must judge whether this is a failure of the treatment, a failure of delivery of the treatment, or that the target population was poorly defined or indeed inappropriate to test the trial hypothesis.

PHYSIOLOGIC AND CLINICAL AND OUTCOMES

Sleep Quality, Gas Exchange, Pulmonary Function, Drive to Breathe, and Mortality

Correction of sleep-disordered breathing associated with obesity-related chronic respiratory failure has been demonstrated in small nonrandomized studies with both continuous PAP (CPAP) and noninvasive ventilation (NIV). These have both been shown to abolish apneic events, consolidate sleep architecture with improvements in slow wave and rapid eye movement (REM) sleep, and improve oxygenation.[7,8] CPAP and NIV have also been shown in these studies to reduce the arousal index and to improve subjective sleep quality.[9] However, there have been no sham-controlled trials and only a single randomized controlled trial that investigated the effect of NIV on sleep quality.[10] Borel and colleagues compared life style advice to treatment with NIV in 35 patients with mild OHS over a 4-week period. The authors demonstrated improvements in the apnea–hypopnea index (AHI), nadir oxygen saturation, mean oxygen saturation, stage 1–2 sleep, REM sleep, and respiratory arousals in the patients randomized to receive NIV (**Fig. 1**). Interestingly, there was no difference in total sleep time (TST) between the groups, but there was an increase in nonrespiratory arousals in the NIV group compared with those patients who received lifestyle counseling alone. This was explained by mask leak-related arousals, and although the difference in nonrespiratory arousals reached statistical significance, the magnitude of difference was small and was greatly outweighed by the clinical improvements in other sleep parameters.

Several studies have compared the efficacy of NIV or CPAP, but only 1 randomized controlled trial has directly compared the 2 modes in terms of the effect on sleep quality, suggesting some subtle benefits in favor of NIV over CPAP.[11] The study, however, was not designed or powered to test for these effects, so other data must be examined to evaluate the potential advantages of each form of PAP in the different manifestations of sleep-disordered breathing in OHS. Banerjee and colleagues[7] used a case-controlled approach to compare the efficacy of CPAP in patients who predominantly had OSA compared to those with OSA plus OHS. Patients were matched for severity of OSA, degree of obesity, and lung volumes based on spirometry. Not unexpectedly, the combined OSA plus OHS group had lower resting daytime and nocturnal oxyhemoglobin saturation by pulse oximetry (SpO_2) levels, and a higher arousal index on diagnostic polysomnography. Despite a similar level of control of upper airway obstruction between the groups in a single-night in-hospital monitored study (AHI OSA group 3.7 $\pm$ 0.9/h vs OSA plus OHS group 3.7 $\pm$ 1.2/h; P = ns), the OSA plus OHS group had more pronounced nocturnal hypoxemia (Nadir SpO_2 OSA group 87 $\pm$ 1% vs OSA plus OHS group 75 $\pm$ 4%, P = .015; %TST SpO_2<90% OSA group 1% [0%–5%] vs OSA plus OHS group 18% [1%–54%], P = .015). The increased nocturnal hypoxemia in this group did not translate into a difference in sleep efficiency between the groups (sleep efficiency OSA group 75 $\pm$ 3% vs OSA plus OHS group 79 $\pm$ 3%; P = ns).

Data suggest that the best predictor of CPAP failure in patients with accompanying OHS is persistent nocturnal hypoxemia despite adequate relief of upper airway obstruction.[12,13] The degree of nocturnal hypoxemia is associated with the ventilatory response to carbon dioxide as evidenced by the assessment hypercapnic ventilatory response (HCVR) before treatment.[8] Indeed, this simple daytime test could be used to clinically stratify patients to optimize treatment with CPAP