EDITORIAL

Chronic Obstructive Pulmonary Disease with Sleep-related Hypoxemia: Nocturnal Oxygen is not the Answer

Tejas M Suri[1], Jagdish C Suri[2]

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Long-term supplemental oxygen therapy (LTOT) provided in a domiciliary setting has been shown to improve survival among patients with chronic obstructive pulmonary disease (COPD) who have severe daytime resting hypoxemia.[1,2] This encompasses patients with arterial oxygen partial pressure (PaO_2) of less than 56 mm Hg (or oxygen saturation (SpO_2) less than 88%) and those with PaO_2 of 56–59 mm Hg with polycythemia or cor pulmonale. However, a significant proportion of COPD patients without severe daytime hypoxemia have nocturnal oxygen desaturation. Significant nocturnal desaturation refers to an SpO_2 of less than 90% more than 30% of the night.[3] In a study of 128 patients with mild-to-moderate daytime hypoxemia (PaO_2 between 56 mm Hg and 69 mm Hg), nocturnal desaturation was observed in 54%. About one-third of these had cyclical desaturations suggestive of obstructive sleep apnea (OSA), whereas two-thirds had sustained nonapneic hypoxemia.[4] Nocturnal oxygen desaturation is associated with cardiac arrhythmias and an increase in pulmonary artery pressure.[5] It is also associated with a rise in inflammatory markers such as high-sensitivity C-reactive protein (hs-CRP) that increases risk of cardiovascular disease.[6] Finally, nocturnal oxygen desaturation in COPD is associated with progression of respiratory failure to requirement for LTOT.[7]

While the overlap syndrome of OSA and COPD is treated with positive airway pressure (PAP) therapy, the optimal treatment for isolated, nonapneic nocturnal hypoxemia in COPD is unknown. Three randomized controlled trials have studied the role of nocturnal oxygen supplementation (targeting SpO_2 greater than 90%) in these patients.[8–10] These trials have failed to show any benefit of nocturnal oxygen therapy in improving survival or preventing progression to LTOT requirement. Although the trials individually had small sample sizes, they collectively conclude that nocturnal oxygen is not beneficial in COPD patients with isolated, nonapneic nocturnal hypoxemia.

In view of the adverse consequences of nocturnal desaturation in COPD, it is important to continue the search for appropriate therapies for these patients. In this regard, it is helpful to revisit the pathophysiology of nocturnal hypoxemia in COPD. Sleep is associated with decreased wakefulness drive to the respiratory system, blunting of hypoxemic and hypercapnic ventilatory responses, and decreased pharyngeal dilator muscle activity with upper airway narrowing.[11] These changes lead to reduced minute ventilation during the sleep. While these changes are inconsequential in healthy individuals, COPD patients with preexisting mild-to-moderate hypoxemia due to ventilation-perfusion mismatch experience precipitous drops in SpO_2 during the sleep. Further, COPD patients with emphysema have downward displacement of the diaphragm that places it at a mechanical disadvantage. These patients are reliant on accessory muscles to supplement their respiratory efforts. Rapid eye movement (REM) sleep results in atonia of the accessory muscles leading to hypoventilation and REM-related desaturations.[11]

Although the aforementioned randomized trials of oxygen supplementation in COPD with nocturnal desaturation excluded OSA patients, they did not evaluate patients for sleep-related hypoventilation prior to enrollment. Further, these trials did not exclude patients with daytime hypercapnia.[8–10] A recent meta-analysis has found that domiciliary noninvasive ventilation (NIV) may improve survival in COPD patients with chronic daytime hypercapnia.[12] Based on this, the American Thoracic Society (ATS) has recommended home NIV therapy in COPD patients with awake $PaCO_2$ greater than 45 mm Hg.[12] Sleep-related hypoventilation (defined as a rise in arterial partial pressure of carbon dioxide ($PaCO_2$) by 10 mm Hg (or >45 mm Hg) for 10 minutes during the sleep) may be a precursor of chronic daytime hypercapnia in COPD patients.[13] Hence, clinical trials of nocturnal NIV in these patients to prevent the progression of respiratory failure and mortality are warranted.

In conclusion, nocturnal oxygen desaturations are common among COPD patients with mild-to-moderate hypoxemia. The nocturnal hypoxemia may be a consequence of OSA or sleep-related hypoventilation. These patients may be considered for polysomnography with transcutaneous capnometry. Those who are diagnosed with COPD-OSA overlap have PAP titration performed and are treated with PAP therapy. Supplemental oxygen is not useful for nonapneic nocturnal hypoxemia and the optimal therapy for these patients is unknown. However, these patients may be evaluated for sleep-related hypoventilation. Clinical trials of NIV therapy are of utmost necessity in COPD

[1]Pulmonary, Critical Care and Sleep Medicine, All India Institute of Medical Sciences, New Delhi, India

[2]Pulmonary, Critical Care and Sleep Medicine, Fortis Flt Lt Rajan Dhall Hospital, Vasant Kunj, New Delhi, India

Corresponding Author: Jagdish C Suri, Pulmonary, Critical Care and Sleep Medicine, Fortis Flt Lt Rajan Dhall Hospital, Vasant Kunj, New Delhi, India, Phone: +91 9810097259, e-mail: docjcsuri@gmail.com

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patients with nocturnal hypoxemia due to sleep-related hypoventilation.

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