

Sleep in COPD

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Introduction

Sleep has well recognized effects on breathing, including changes in central respiratory control, airways resistance and muscular contractility. These physiologic changes do not have any adverse effect in healthy individuals but may have profound effect in gas exchange in patients with COPD.

Sleep is associated with a diminished responsiveness of the respiratory centre in medulla to chemical, mechanical and cortical inputs^{1,2}, particularly during REM sleep. Furthermore, the responsiveness of the respiratory muscles to respiratory centre outputs are also diminished during sleep, particularly during REM, although the diaphragm is less affected than the accessory muscles in this regard².

Because of a marked reduction in intercostal muscle activity (diaphragmatic contraction less affected) a reduction in ribcage contribution to breathing has been reported during REM sleep compared to wakefulness and non-REM sleep³. This fall in intercostal muscle activity assumes particular clinical significance in patients who are particularly dependant on accessory muscle activity to maintain ventilation, such as those with COPD, where lung hyperinflation reduces the efficacy of diaphragmatic contraction⁴.

Hypoxaemia during sleep

All patients with COPD become more hypoxemic during sleep, most marked during REM sleep, than during wakefulness^{5,6,7,8}. The saturation drop in oxygen during

sleep is approximately double that observed during maximal exercise⁹.

A definite relationship exists between oxygenation during wakefulness and that during sleep. Patients who are most hypoxemic when awake are most severely hypoxemic during sleep¹⁰.

Extent of nocturnal hypoxemia relates both to daytime oxygenation and to daytime arterial carbon dioxide tension^{10,11} and the duration of REM sleep¹⁰. Attention has been given to the concept of nocturnal desaturators among patients whose awake arterial oxygen tension is above 60 mm Hg¹². Of 152 such COPD patients, Fletcher & colleagues¹² found that 41 desaturated, when desaturation was defined arbitrarily as having an oxygen saturation below 90% for at least 5 minutes with a trough saturation of 85% or lower¹².

Interestingly, nocturnal desaturators could not be predicted from their lung function or symptoms. Their mean PaO₂ during wakefulness was significantly lower (70 vs 78 mmHg) and PaCO₂ was higher (41 vs 38 mmHg) than those who did not desaturate during sleep.

Sleep related hypoxemia and hypercapnia are well recognized in COPD particularly during REM sleep and may contribute to the development of cor pulmonale¹³ and nocturnal death¹⁴. These abnormalities are more common in "blue bloaters" than "pink puffers"^{2,13}. However, many patients with awake PaO₂ in the mildly hypoxemic range can also develop substantial nocturnal oxygen desaturation, that appears to predispose to pulmonary hypertension⁵.

Mechanism of hypoxemia during sleep in COPD

A. Hypoventilation

In most patients with COPD, nocturnal hypoxemia is

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associated with continued ventilation and not with apnoea^{16,17,18,19} unless the patient has associated sleep apnoea. Ventilation is lower during all stages of sleep compared with wakefulness in normal subjects⁶ and also in patients with COPD. During REM sleep, breathing patterns are similar in patients with COPD and normal subjects²⁰. In normal subjects alveolar ventilation may be about 40% lower during bursts of eye movements in REM sleep, than during wakefulness^{20,21}. Because patients with COPD have greater dead space, such rapid, shallow breathing would be expected to produce an even greater decrease in alveolar ventilation than occurs in normal subjects. Hypoventilation during sleep is due to a combination of factors. In non-REM sleep, ventilation drops because of decreased BMR²² and ventilatory drive²³ and an increase in upper airway resistance²⁴. During REM sleep, brain stem function is altered with phasic activity of respiratory neurons, at least in animals²⁵. During REM sleep there is also hypotonia of the intercostals, an accessory muscles of inspiration⁴, resulting in a decreased contribution of the ribcage to ventilation^{26,27}. This has a particularly marked effect on the ventilation in hyperinflated patients with COPD, in whom the flattened diaphragm—the major active respiratory muscle in REM sleep—pulls in the flattened lower chest wall, resulting in inefficient ventilation. This may explain why COPD patients may become more hypoxemic than patients with fibrotic lung disease during sleep²⁸. REM hypoventilation is accompanied by decrease in both hypoxic^{23,29} & hypercapnic^{30,31} ventilatory response.

B. Ventilation / perfusion mismatch

That additional ventilation / perfusion mismatch occurs in COPD during the marked hypoventilation of REM sleep is supported by the fact that cardiac output is unchanged during REM hypoventilation indicating alteration in global ventilation / perfusion matching^{17, 32}. It has been found that transcutaneous PCO₂ level rises to a similar extent in those patients who developed major nocturnal desaturation as those who developed only a minor degree of desaturation⁹. This suggests a similar degree of hypoventilation in both the groups, despite the different degrees of nocturnal oxygen desaturation. The much larger fall in PaO₂ among the major desaturators as compared with minor desaturators, in conjunction with similar rise in transcutaneous PCO₂

in both the groups, suggests that in addition to a degree of hypoventilation operating in all patients, other factors such as mismatching must also play a role in the excess desaturation of some COPD patients.

C. Coexisting sleep apnoea (overlap syndrome)

The incidence of sleep apnoea in patients with COPD is about 10-15%^{33,34} which is higher than would be expected in a normal population of similar age. Impaired respiratory drive may predispose to sleep apnoea in COPD patients, particularly the blue-boater types. Patients with coexisting COPD and sleep apnoea typically develop more severe hypoxemia during sleep because such patients may be hypoxemic at the commencement of each apnoea, whereas patients with only sleep apnoea tend to resaturate in between the apneas. Therefore, they are more prone to the complications of chronic hypoxemia such as cor-pulmonale or polycythemia.

Consequences of sleep hypoxemia

A. Haemodynamic

Pulmonary artery pressure rises during sleep in patients with COPD^{5,6,17,32,35}. In 12 patients with COPD, mean pulmonary arterial pressure rose from 37mm of Hg during wakefulness to 55 mm of Hg during REM sleep as average arterial oxygen tension fell from 56 to 43 mm of Hg⁵. During those episodes, cardiac output increases little, if at all^{17,32}.

B. Red cell mass

Morning erythropoetin levels have been found to be increased in some patients with COPD^{36,37} and nocturnal erythropoetin may rise in COPD patients whose SaO₂ falls below 60% at night³⁸. Nocturnal desaturators (as defined earlier) had higher daytime pulmonary artery pressure and red cell mass than nondesaturators³⁹.

C. Cardiac dysrhythmia

COPD patients have more ventricular ectopics during sleep^{40, 41}.

D. Sleep quality

Patients with COPD sleep badly compared with healthy subjects as assessed by either symptoms⁴² or EEG recording^{43,44,45}.

E. Death during sleep in COPD

Death is more common by night than by day in patients with COPD⁴⁶ particularly in those with CO₂ retention and hypoxemia where nocturnal O₂ therapy reduces frequency of nocturnal deaths⁴⁷.

F. Consequences of OSA combined with COPD

These patients are more prone to developing pulmonary hypertension⁴⁸, right heart failure^{49,50} & CO₂ retention⁵¹ than patients with OSA without lung disease.

Investigations of sleep related breathing disturbances in COPD

It is now widely accepted that sleep studies are not routinely indicated in patients with COPD, particularly since the awake PaO₂ level provides a good indicator of the likelihood of nocturnal oxygen saturation^{10,52}. Sleep studies are indicated only when there is a clinical suspicion of OSA or manifestations of hypoxemia not explained by awake PaO₂ level, such as cor-pulmonale or polycythemia.

Treatment of nocturnal hypoxemia in COPD

A. Oxygen therapy

Nocturnal oxygenation in patients with COPD is improved by nocturnal oxygen therapy⁶. The concentration of added oxygen should be carefully titrated to bring the PaO₂ up into the mildly hypoxemic range (as the respiratory drive in such patients may be dependent on stimulant effect of hypoxemia) in order to minimize the tendency to CO₂ retention, particularly during sleep⁵³. However the risk of CO₂ retention with supplemental O₂ therapy in such patients may have been overstated in the past and some reports have found that CO₂ retention with oxygen supplementation is often modest and usually nonprogressive⁵⁴.

B. Non-invasive positive pressure ventilation (NIPPV)

NIPPV has the theoretical advantage over long term oxygen therapy of reducing rather than raising arterial CO₂ tension. NIPPV plus oxygen therapy, however produce greater improvements in daytime PaO₂ and PaCO₂ and overnight PaCO₂, sleep quality than oxygen therapy alone in a randomized controlled trial of 14 COPD patients⁵⁵. NIPPV has been shown to reduce the need for intubation and mechanical ventilation in patients of COPD with acute exacerbation and associated with respiratory failure⁵⁶.

C. Respiratory stimulants

Although almitrine, protryptine, acetazolamide have effects in improving oxygenation and reducing Co₂ tension during night, their long term administration has not been recommended.

D. Alcohol

Patients with COPD should be advised not to drink alcohol, particularly in the evening as it may worsen hypoxemia⁵⁷.

E. Inspiratory muscle training

This may improve nocturnal oxygenation in patients with COPD⁵⁸.

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