Chest Heart Journal
Vol. 46, No. 2, July 2022

REVIEW ARTICLE

COPD and Obstructive Sleep Apnea (OSA) - The Overlap Syndrome

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Abstract

Chronic obstructive pulmonary disease (COPD) and obstructive sleep apnea (OSA) are highly prevalent disorders and the co-existence of both disorders, termed the overlap syndrome (OS). Patients with OS have a substantially greater risk of morbidity and mortality, compared to those with either COPD or OSA alone. Keeping in mind the risk of mortality, it is crucial for clinicians to clinically evaluate the patients with OSA or COPD for the occurrence of overlap syndrome and provide effective treatment options for the same. This review aims to highlight the pathophysiology and the risks associated with the OS along with early detection and appropriate management protocols to reduce the mortality associated with it.

[Chest Heart J. 2022; 46(2) : 89-93]

DOI: http://dx.doi.org/10.33316/chab.j.v46i2.2019658

Introduction and Background

The term overlap syndrome (OS) was coined by David C. Flenely in 1985 to describe the association between obstructive sleep apnea (OSA) with breathing disorders like chronic obstructive pulmonary disease (COPD) in a patient[1].

The prevalence of overlap syndrome varies among geographic regions and populations[2]. Shawon et al reported incidences of COPD coexisting with OSA ranging from 2.9% to 65.9% in a systematic review.

During sleep, patients with COPD experience nocturnal hypoxemia and hypoventilation mainly during the rapid eye movement (REM) phase of the sleep due to relaxation of intercostal muscles and reduced chest wall mobility. On the other hand, patients with OSA experience episodes of apnea and hypopnea mainly through upper airway collapse, reduced intrathoracic pressures, and activation of the sympathetic nervous system resulting in nighttime arousals and excessive daytime sleepiness[3]. These episodes of nocturnal oxygen desaturation (NOD) with hypercapnia and hypoxemia are more profound in patients with overlap syndrome in comparison to COPD or OSA alone. The overlap syndrome may further increase the risk of cardiovascular events particularly pulmonary hypertension and atrial fibrillation, thereby resulting in poor outcome and increased risk of mortality than in patients with COPD or OSA alone.

Factors in COPD that influence the potential for OSA

Complex interaction between sleep, bodymass index, and COPD may either prevent or promote development of OS. Patients with COPD with

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Submission on: 8 June, 2022 **Accepted for Publication:** 22 June, 2022
Available at http.//www.chabjournal.org

predominant emphysema and severe airflow obstruction may be protected against developing OSA. This is because the hyperinflated emphysematous lungs reduce the collapsibility of the upper airways by a caudal traction effect. Patients with severe COPD and emphysema also have lower body mass indices (BMIs), which is also protective against OSA[4]. In contrast, patients with relatively mild COPD who have a higher BMI tend to develop OSA, leading to the OS at a younger age[5]. These patients may be heavy smokers with higher cumulation of pack-years, which contributes to upper airway inflammation and OSA[6]. Furthermore, they often develop right heart failure at an earlier age. These patients experience rostral fluid shifts at night which worsens obstructive events due to edema of neck structures.

Clinical consequences of overlap syndrome

Patients with OS have increased risk of mortality due to cardiovascular events . Hypoxic drive results in oxidative stress and stimulates the release of systemic inflammatory mediators like TNF-á, IL-6, IL-8, CRP which ultimately results in endothelial dysfunction and atherosclerotic plaque formation[7].

OS also results in metabolic dysfunction including insulin resistance and abnormal lipid metabolism. OS is also associated with systemic hypertension which increases the risk of coronary artery disease, congestive heart failure, arrhythmias and stroke[8].

Patients with OS have increased risk of pulmonary hypertension and right heart failure. Hawrylkiewicz et al. observed in their study that 86% subjects with OS had pulmonary hypertension as compared to 16% subject with OSA alone[9].

Diagnosis of overlap syndrome

There is no formal guidance for the indications of performing a sleep study in patients with COPD. Extrapolating from the ATS guidelines for hypercapnic COPD patients, it is reasonable to consider diagnostic testing in COPD patients with an intermediate-to-high risk for OSA using the STOP-BANG questionnaire score[10]. Furthermore, COPD patients with pulmonary hypertension and borderline or nocturnal hypoxemia can be considered for sleep study. In-lab attended polysomnography with PAP titration is the gold standard for the diagnosis and treatment of OS.

Overlap syndrome is amenable to phenotyping

Figure 1 shows that patients with COPD may suffer from a spectrum of sleep related breathing disorder (SRBD), the exact nature of which depends on the relative severity of the emphysema and obesity. Patients with emphysema have higher sleep-related hypoventilation due to the mechanically disadvantaged downwardly displaced diaphragm, but they are protected against OSA because of low

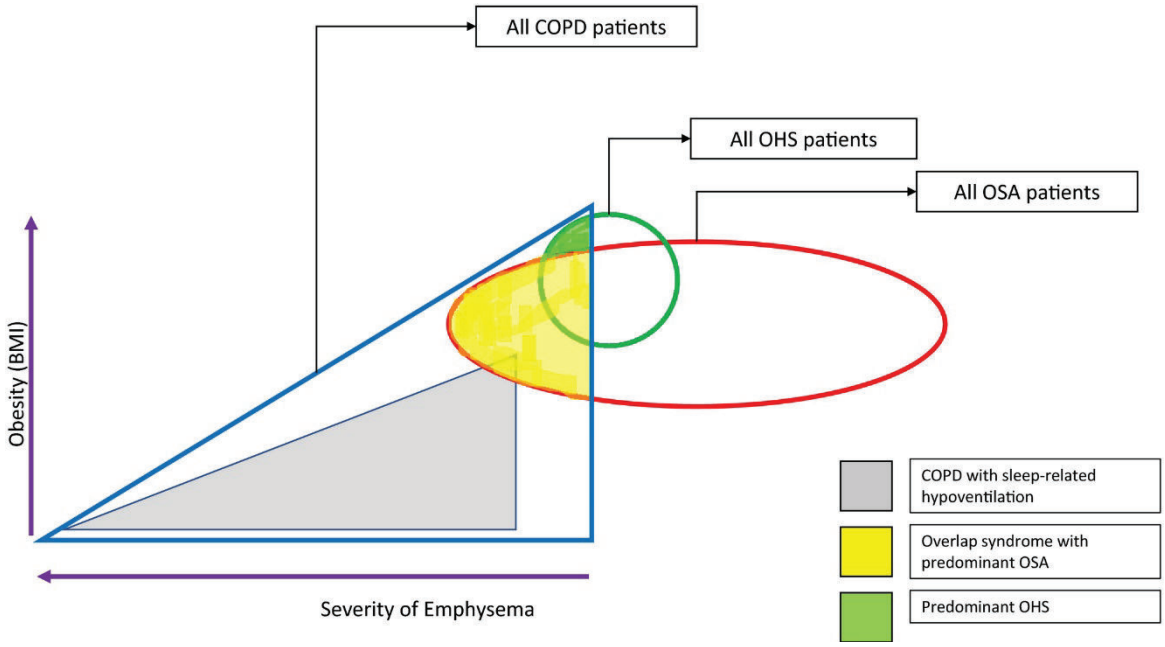

Fig.-1: *Proposed phenotypic classification of sleep-related breathing disorders (SRBD) in Chronic Obstructive Pulmonary Disease.*

BMI and caudal traction on the upper airways. In contrast, patients with obesity tend to have predominant OSA or OHS.

Management

Treatment of the overlap syndrome largely does not differ from treatment of the constituent diseases. The goal of treatment is to maintain adequate oxygenation at all times and to prevent sleep-disordered breathing disorder.

EVIDENCE FOR THE USE OF PAP THERAPY IN OVERLAP SYNDROME

To date, only observational studies of PAP therapy in OS patients have been conducted. PAP therapy in OS patients has been found to reduce pro-inflammatory markers implicated in cardiovascular disease, including C-reactive protein (CRP) and tumor necrosis factor-á[11]. PAP therapy has been linked with physiological benefits in OS including improved arterial blood gases (reduced PaCO2 and increased PaO2)[12].

Currently, there is no formal guidance for the use of PAP therapy in patients with COPD and SRBD. In the absence of well-designed RCTs, our understanding is limited to large observational studies and extrapolations of evidence from related conditions such as OSA, COPD with chronic hypercapnia and OHS. We have presented a decision-tree of a proposed phenotypebased management algorithm of SRBD in COPD (Figure-2)

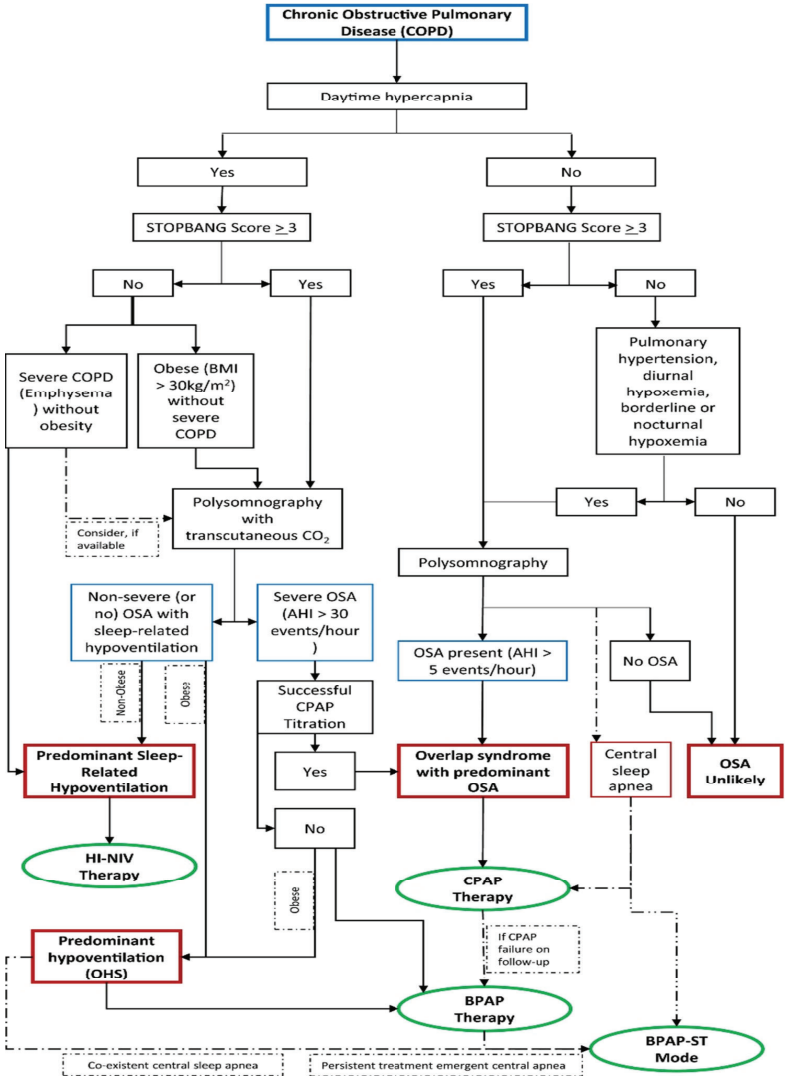

Fig.-2: *phenotype-guided approach toward the diagnosis and positive airway pressure therapy of sleeprelated breathing disorders with Chronic Obstructive Pulmonary Disease.*

OTHER THERAPIES FOR OVERLAP SYNDROME

Lifestyle Modifications

Structured exercise program and pulmonary rehabilitation are shown to be beneficial in both OSA and COPD. Structured exercise programs aim to improve the skeletal muscle wasting in patients with COPD. Likewise, structured exercise program in OSA patients have shown improvement in AHI, daytime sleepiness, and overall sleep quality[13].

Supplemental Oxygen Therapy

Studies have shown that supplemental oxygen therapy for more than 18 hours a day including during sleep can help to improve daytime and nocturnal hypoxemia and reduce the risk of mortality in these patients.

Bronchodilators and Corticosteroids

Treatment of the underlying obstructive lung disease is helpful in preventing or ameliorating nocturnal oxygen desaturation in those with COPD.

Bi-level PAP

The effects of bi-level PAP on overlap syndrome have not been specifically evaluated. However, one study that found benefit from NIV in hypercapnic COPD may have included overlap-syndrome patients[14]. Whether longterm NIV would improve outcomes in the overlap syndrome, compared to CPAP, perhaps in addition to supplemental oxygen, is unknown.

Conclusions

Keeping in mind the increased risk of cardiovascular morbidity and mortality with OS, it is important for clinicians to screen COPD patients with OSA and vice versa. Patients with a high index of suspicion should be clinically assessed and advised effective treatment options for the same. A phenotype-based approach of selecting PAP therapy which is tailored to correct the pathophysiology of SRBD demonstrates potential to improve clinical outcomes. To strengthen the evidence base, additional research is needed in the form of well-designed clinical trials which use the phenotypic approach to the management of OS and SRBD in COPD.

Reference

1 Flenley DC: Sleep in chronic obstructive lung disease . Clin Chest Med. 1985, 6:651-61.

2 Shawon MS, et al. Current evidence on prevalence and clinical outcomes of co-morbid obstructive sleep apnea and chronic obstructive pulmonary disease: a systematic review. Sleep Med Rev. 2017;32:58–68.

3 Epstein LJ, Kristo D, Strollo PJ Jr, et al.: Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. J Clin Sleep Med. 2009, 5:263-276

4 Wu Z, Yang D, Ge Z, Yan M, Wu N, Liu Y. Body mass index of patients with chronic obstructive pulmonary disease is associated with pulmonary function and exacerbations: a retrospective real world research. J Thorac Dis. 2018;10(8):5086-5099. https://doi. org/ 10.21037/jtd.2018.08.67.

5 Xiong MQ, Hu WH, Hu K, et al. Analysis of risk factors and consequences for concurrent obstructive sleep apnea in chronic obstructive pulmonary disease patients. Zhonghua Jie He He Hu Xi Za Zhi Zhonghua Jiehe He Huxi Zazhi Chin J Tuberc Respir Dis. 2019;42(11):832-837. https://doi.org/10.3760/ cma.j.issn.100 1-0939.2019.11.009

6 Lin Y-N, Li Q-Y, Zhang X-J. Interaction between smoking and obstructive sleep apnea: not just participants. Chin Med J (Engl). 2012;125(17):3150-3156

7 Fletcher EC, Schaal JM, Miller J, Fletcher JG: Long-term cardiopulmonary sequelae in patients with sleep apnea and chronic lung disease. Am Rev Respir Dis. 1987, 135:525-533

8 Somers VK, White DP, Amin R, et al.: Sleep apnea and cardiovascular disease. J Am Coll Cardiol. 2008, 52:686-717

9 Hawrylkiewicz I, Sliwinski P, Gorecka D, Plywaczewski R, Zielinski J: Pulmonary haemodynamics in patients with OSAS or an overlap syndrome. Monaldi Arch Chest Dis. 2004, 61:148-152. 10.4081/monaldi.2004.693

10 Macrea M, Oczkowski S, Rochwerg B, et al. Long-term noninvasive ventilation in chronic

stable hypercapnic chronic obstructive pulmonary disease. an official american thoracic society clinical practice guideline. Am J Respir Crit Care Med. 2020;202(4):e74- e87. https://doi.org/10.1164/rccm.202006-2382ST

11 Wang Y, Su M, Zhang X. Effects of continuous positive airway pressure treatment of inflammatory factors in patients with overlap syndrome. Zhonghua Yi Xue Za Zhi. 2014;94(6):416–419. https:// doi.org/10.3760/CMA.J.ISSN.0376-2491.2014.06.005

12 de Miguel J, Cabello J, Sánchez-Alarcos JMF, Alvarez-Sala R, Espinós D, Alvarez-Sala JL. Long-term effects of treatment with nasal continuous positive airway pressure on lung function in patients with overlap syndrome. Sleep Breath Schlaf Atm. 2002;6(1):310. https://doi.org/10.1007/s11325-002-0003-6

13 Sengul YS, Ozalevli S, Oztura I, Itil O, Baklan B: The effect of exercise on obstructive sleep apnea: a randomized and controlled trial. Sleep Breath. 2011, 15:49-56. 10.1007/s11325-009-

14 Meecham Jones DJ, Paul EA, Jones PW, Wedzicha JA. Nasal pressure support ventilation plus oxygen compared with oxygen therapy alone in hypercapnic COPD. Am J Respir Crit Care Med 1995; 152(2):538-544