ISSN: 0975-833X

Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 8, Issue, 06, pp.33340-33344, June, 2016

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

RESEARCH ARTICLE

AHI AND NOCTURNAL DESATURATION IN COPD PATIENTS: AN EARLY INDICATOR FOR LTOT/ CPAP THERAPY

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ARTICLE INFO

Article History:
Received 14th March, 2016
Received in revised form
26th April, 2016
Accepted 21st May, 2016
Published online 30th June, 2016

Key words:

AHI, COPD,
Overlap syndrome,
Nocturnal desaturation,
Hypoxemia,
Long-term oxygen therapy.

ABSTRACT

COPD patients breathe against expiratory obstruction with low tidal volume and have ineffective ventilation while asleep. Such patients are at higher risk of developing nocturnal desaturation, which is considered a major determinant of disturbed sleep among COPD patients. However, nocturnal desaturation in each COPD patients depends upon severity of the disease.

Early detection of night time desaturation in COPD patients can prevent further complications associated with hypoxemia like cor Pulmonale, pulmonary hypertension etc., by initiation of low flow nocturnal oxygenation. We conducted a pilot project in which 30 stable COPD patients fulfilling inclusion criteria were enrolled after obtaining an informed written consent. Out of 30 COPD patients, 6 had mild obstruction, 19 had moderate obstruction and 5 had severe obstruction with poor reversibility on PFT. Our results showed that Patients who had nocturnal spo2 below 85%:1 of 30 patients (3.33%) mild, 14 of 30(46.67%) moderate, 6 of 30 (20%) had severe COPD, spo2 between 85-90% :2 of 30 patients (6.67%) moderate, spo2 between90-95% : 4 of 30 patients (13.33%) mild, 1 of 30 (3.33%) moderate, spo2 between 95-100% : 1 of 30(3.33%) each had mild and moderate COPD. Out of 30 COPD patients 23 had OSA, of which 4 patients (17.33%) had normal BMI and 19 patients (82.6%) were overweight.

Citation: Dr. Pranali Patil, Dr. Jayalakshmi, T. K., Dr. Abhay Uppe, Dr. Girija Nair and Dr. Pragati Agrawal, 2016. "AHI and nocturnal Desaturation in COPD patients: An early indicator for LTOT/ CPAP therapy", *International Journal of Current Research*, 8, (06), 33340-33344.

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is associated with significant morbidity and mortality. It is currently the fourth leading cause of death in the United States and is expected to increase to the third leading cause by the year 2020 (Barnes, 2000; Hurd, 2000). Unrecognised Nocturnal desaturation with and/or without daytime desaturation is a major cause of concern for clinicians. COPD patients are at risk for hypoventilation during sleep due to the underlying respiratory dysfunction. The worsening of hypoxemia during sleep in patients with chronic obstructive pulmonary disease (COPD) has been documented since the early 1960s (Trask and Cree, 1962), and has since been confirmed by polysomnograhy studies (Koo *et al*., 1975; Leitch *et al*., 1976), which have included continuous monitoring of oxygen saturation from the late 1970s (Flick and Block, 1977; Wynne *et al*., 1979; Douglas *et al*., 1979; Littner *et al*., 1980; Fleetham *et al*., 1982; Calverley *et al*., 1982; Catterall *et al*., 1983).

It must be emphasized that most of these studies have included patients with severe COPD exhibiting marked daytime hypoxemia. Several studies of the literature have shown that a relatively high percentage of these COPD patients exhibit significant nocturnal hypoxemia, which raises query, whether to start low flow nocturnal oxygenation in such candidates (Fletcher *et al*., 1987; Levi-Valensi *et al*., 1992; Mulloy and McNicholas, 1996). COPD patients frequently complain of poor sleep quality and inadequate sleep (Calverley 1982; Cormick 1986). Some of the factors leading to sleep disruption in COPD patients may also be related to the worsening of respiratory function during sleep, which may result from nocturnal hypoventilation, ventilation-perfusion mismatch, and decreased functional residual capacity. Though decreases in nocturnal oxyhemoglobin saturation (SaO2) may occur during sleep in COPD patients, the episodes tend to be more pronounced during rapid eye movement (REM) stages of sleep due to loss of peripheral muscle tone and a functional dependence on an impaired flattened diaphragm (Douglas 1979; Stradling 1983; George 1987). (Ana C Krieger *et al*., 2007)

Four studies have examined the effects of nocturnal desaturation and its correction with oxygen therapy on sleep architecture and quality in OSA patients without COPD. (Calverley *et al*., 1982; Fleetham *et al*., 1982; Goldstein *et al*., 1984; McKeon *et al*., 1989) These studies were small, short term and sleep laboratory based, employed variable methodology and produced differing results. Only one study attempted to evaluate longer term sleep quality via questionnaires, but aside from this the effects of nocturnal desaturation in COPD, sleep quality and daytime function have not been studied. Indian literature does not reveal any studies correlating AHI, Nocturnal desaturation in stable COPD patients, however one study show The severity of exacerbation in COPD due to the overlap of obstructive sleep apnoea syndrome (OSAS). (Acute exacerbation of COPD in relation to overlap syndrome, 2015) The paucity of data on the prevalence and clinical impact of isolated nocturnal desaturation is reflected in the recent NHLBI research work shop report on supplementary oxygen therapy in COPD, which identified the clinical implications of nocturnaldesaturation as one of four areas of oxygen research requiring urgent further study.[19,20] The aims of this study were, firstly whether COPD patients show nocturnal desaturation which is associated with or without day time hypoxemia, secondly to determine, if there is correlation between the degree of desaturation and the severity of COPD and contribution of COPD –OSA syndrome in nocturnal desaturation. In this study, we used the nasal cannula/pressure transducer system to evaluate respiratory events and oxyhemoglobin desaturation in COPD patients referred for evaluation of sleep-disordered breathing. Our study included a group of COPD patients with and without daytime hypoxemia.

MATERIALS AND METHODS

Our study included 30 stable and previously diagnosed COPD patients attending OPD and INPATIENTS at D.Y. Patil University School of Medicine, Hospital and Research Centre, fulfilling inclusion criteria and enrolled after obtaining an informed written consent. Complete history, detailed physical examination detailed evaluation of sleep was followed by investigations like chest x-ray, PFT, 2D ECHO, polysomnography. Inclusion criteria included only those patients of COPD whose daytime oxygen saturation was more than 95% at rest.

Exclusion criteria were:

(1) All patients whose daytime oxygen saturation at rest less than 95%
(2) Current or past use of continuous positive airway pressure, bi-level or supplemental oxygen;
(3) Respiratory failure requiring hospitalization within the previous 8-weeks; and
(4) Diagnosis of anemia.
(5) Patients were excluded from the study if they had left heart or congenital heart diseases, associated lung diseases (ILD, Bronchiectasis, lung carcinoma) or other severe diseases that could influence survival (hepatic cirrhosis, chronic renal failure)

The room air oxyhemoglobin saturation (RA) SaO_2, FEV1 and FEV1/FVC were recorded during spirometry. Subsequently, all patients were administered the Epworth Sleepiness Scale (ESS) in order to assess daytime sleepiness (Johns 1991). An attended nocturnal polysomnography was performed in all patients at their approximate routine sleeping hours. Recorded channels included electroencephalogram, bilateral electrooculogram (EOG), submental and anterior tibialis electromyogram (EMG), ECG, rib cage and abdominalmotion by inductive plethysmography, body position, nasal cannula/pressure transducer system for respiratory monitoring and oximetry with digital signal extraction. This oximetry technology was chosen because it is based on real time acquisition and processing of SaO2 data and because it has improved detection in states of low perfusion, motion, and weak signal. PSG machine used, Alice 6 LDxN, Sleep ware G3 Philips Respironics.

Ethics

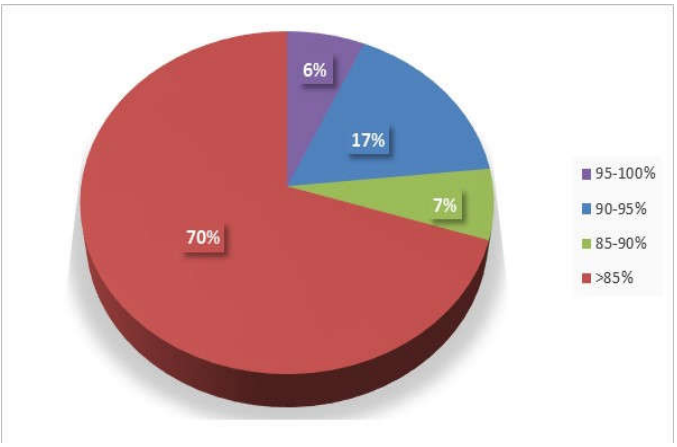
The procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation.

Statistics

All respiratory events were tabulated (apnoea, hypopnea, and RERA) and calculated to a final hourly index of events. Decreases in oxyhemoglobin saturation were recorded. Data from the study was tabulated, and analysed by plotting it on x-axis and y with respective parameters. / Data has been tabulated and values put against x and Y axis to obtain results

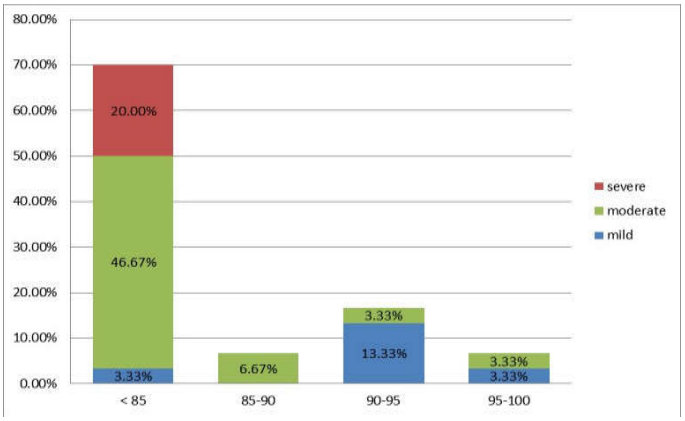
RESULTS

Out of 30 COPD patients, 6 had mild obstruction, 19 had moderate obstruction and 5 had severe obstruction with poor reversibility on PFT.



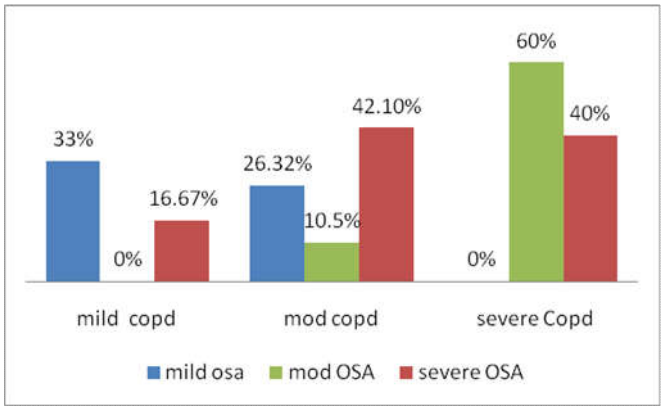
(Graph 1)

1.Nocturnal desaturation: out of 30, 2(6%) desaturated between 95-100 %, 5(17%) between 90-95%, 2(7%) between 85-90%, 21(70%) pts desaturated < 85% (graph 1)



(Graph 2) X axis- patients nocturnal SpO_2, Y axis – total number of patients

- Patient desaturated below 85% - 1 of 30 patients (3.33%)mild COPD,14 of 30 (46.67%) moderate COPD, 6 of 30 (20%) were severe COPD
- Patient desaturated between 85-90% - 2 of 30 patients (6.67%) moderate COPD
- Patient desaturated between 90-95% - 4 of 30 patients (13.33%) mild, 1 of 30 (3.33%) moderate COPD
- Patient desaturated between 95-100% - 1 of 30 patients (3.33%) each were mild and moderate COPDs



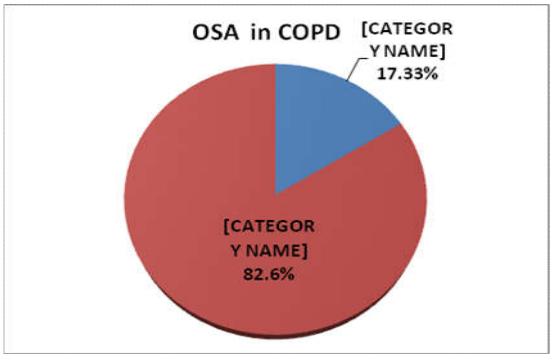
(Graph 3) X axis- COPD patients with OSA, Y axis – total number of patients

- AHI/ OSA in COPD (severity): 2/6 (33%) mild COPD had mild OSA (overlap syndrome).
- 5/19 (26.32%) moderate COPD showed mild OSA, 2/19 (10.5%) moderate COPD showed moderate OSA, 8/19(42.1%) moderate COPD showed severe OSA, 6/11 (54.5%) of moderate COPD showed severe OSA.
- 3/5 (60%) severe COPD showed moderate OSA and 2/5 (40%) severe COPD showed severe OSA. (Graph 3)

(Graph 4) BMI in COPD patients with OSA

BMI and COPD SEVERITY

Out of 30 COPD patients 23 had OSA, of which 4 patients (17.33%) had normal BMI and 19 patients (82.6%) were overweight. (Graph 4)



(Graph 4) BMI in COPD patients with OSA

DISCUSSION

Many patients with COPD have poor sleep quality, especially those who have high anxiety and depression, the anxiety experienced due to dyspnoea affects the sleep quality of patients with COPD and the sleep quality has effects on physical and emotional functions. COPD-related sleep disturbances play a role in its morbidity and adversely affect quality of life. Poor sleep quality could contribute to poor COPD-related outcomes such as exacerbations or even mortality risk. (Flenly, 1978; Fletcher, 1986) Sleep-disordered breathing (mainly obstructive sleep apnea (OSA)) and COPD are among the most common pulmonary diseases. Although they may have common pathophysiological mechanisms, even by chance alone, asubstantial number of patients will have both OSA and COPD—what Flenley termed "the overlap syndrome." A study regarding COPD and nocturnal desaturation showed 33 of the 42 patients had one or more nocturnal desaturations, and in 10 patients, mean nocturnal oxygen saturation was below 90% (VOS 1995) In another study, out of 94 COPD patients 66 were desaturators (Chaouat, 1997). In our study, out of 30 patients 21 desaturated below 85%, of which 1 mild, 14 moderate and 6 had severe COPD. 2 Patients showed nocturnal SpO_2 between 85-90%, and had moderate COPD. Out of 30 patients 23 showed desaturation below 90% of which 1 had mild, 16 had moderate and 6 had severe COPD.

Mechanism of oxygen Desaturation during sleep in COPD patients

Sleep is a physiological situation that occurs depending on the special functional organization of the central nervous system. Normal sleeping is divided into non-rapid eye movement (NREM) and rapid eye movement (REM). NREM consists of three stages: N1, N2 and N3 (quiet sleep or delta sleep).During NREM sleep, the metabolic demand of the brain decreases and the blood flow throughout the entire brain progressively decreases. While metabolic rate decreases during sleep, responses to various chemical, mechanical, and cortical stimuli also decrease. The respiratory response to the changes observed in the partial oxygen and partial carbon dioxide pressures in the arterial blood differs significantly in comparison to the wakefulness period. Especially during REM sleep, such physiological changes may affect gas exchange, hypoxemia can reach critically low levels, especially in patients with already borderline waking oxygenation, and lead to hypoventilation resulting in clinically significant hypoxemia and hypercapnia in

patients with COPD and leads to clinical consequences such as cardiac dysrhythmias, pulmonary hypertension, and polycythaemia. (Fletcher *et al*., 1983) In COPD, breathing against expiratory airflow obstruction becomes more difficult during sleep when there is reduced tidal volume, ineffective ventilation, and hypoxemia. The oxygen desaturation which occurs during sleep in COPD may be greater than that which occurs during maximal exercise (Fletcher *et al*., 1983). Reduction in ventilation is accompanied by deranged ventilation/perfusion (V/Q mismatch) and adequate gas exchange does not occur. As a result, arterial oxygen decreases and carbon dioxide increases. (Fletcher *et al*., 1983) In COPD patients, this hypoxemia is associated with rise in pulmonary arterial pressures and premature ventricular contractions (Fletcher *et al*., 1983) which tend to increase during sleep, and is reversed with oxygen treatment. (Fletcher *et al*., 1987; Block *et al*., 1979; Nattie *et al*., 1978) However, in patients who suffer from both COPD and sleep apnoea, apnoea associated oxygen desaturation is more profound and longer because these patients are already hypoxic when the apnoea begins. In our study Out of 30 patients 23 showed nocturnal desaturation below 90%, who do not fit into conventional LTOT criteria are eligible for oxygen therapy. Long term oxygen therapy (LTOT) refers to the provision of oxygen therapy for continuous use at home for patients with chronic hypoxaemia (PaO_2 at or below 7.3 kPa, (55mHg). The oxygen flow rate must be sufficient to raise the waking oxygen tension above 8 kPa, (60 mmHg). Once started, this therapy is likely to be lifelong. LTOT is usually given for at least 15 hours daily, to include night time, in view of the presence of worsening arterial hypoxaemia during sleep. (Clinical component for the home oxygen service in England and Wales, BTS, 2006)

Indications

At least two arterial blood gas determinations while breathing room air for at least 20 minutes showing PaO_2< or equal to 55 %

1. At rest in non-recumbent position, the PaO2 of 55mmHg or less, SpO2 < 88% on RA (GOLD, The Global Strategy for Diagnosis, Management and Prevention of COPD, 2016)
2. Patients with PaO2 > 55 mmHg & / Spo2 > 88-89% are considered in the following conditions:

(a) Patient on optimal medical treatment with demonstrable hypoxic organ dysfunction, such as secondary pulmonary hypertension (GOLD, The Global Strategy for Diagnosis, Management and Prevention of COPD, 2016), cor Pulmonale (GOLD, The Global Strategy for Diagnosis, Management and Prevention of COPD, 2016), polycythaemia or CNS dysfunction;

(b) When there is a demonstrable fall in PaO2 below 55 mmHg during sleep, associated with disturbed sleep pattern, cardiac arrhythmias or pulmonary hypertension. These patients may be benefited by nocturnal oxygen therapy.

Out of 30 COPD patients 23 had OSA, of which 4 patients (17.33%) had normal BMI and 19 patients (82.6%) were overweight. CPAP remains the accepted standard treatment for OSA, and currently is the accepted standard for overlap syndrome. But CPAP alone may not fully correct hypoxemia, so supplemental oxygen may be required (GOLD, The Global Strategy for Diagnosis, Management and Prevention of COPD, 2016). Controversyexists as to whether CPAP therapy improves daytime lungfunction in those with stable COPD. According to a study in the Journal of Clinical Sleep Medicine, another benefit of CPAP therapy is a lower risk of mortality in patients who have COPD and sleep apnea. Researchers found that people with both conditions who used CPAP more than two hours a night tended to live longer than those who used the therapy less than two hours a night. Studies also noted that CPAP was especially beneficial to COPD patients already on long-term oxygen therapy. Machado and colleagues added the use of CPAP to long-term oxygen therapy and observed differences in long term survival of 71% versus 26%. (Sampol *et al*., 1996) As per Marine *et al*., CPAP reduces exacerbation rates for concurrent COPD. (Machado *et al*., 2010) However, the optimal prescription for CPAP was unclear. Their patients were included in the group if they used CPAP ≥ 4 h/night and, if not, the device was withdrawn. Similar to the Spanish study, their analysis shows an association with high mortality when CPAP use is < 4 h/night. (Marin *et al*., 2010)

Conclusion

1. Nocturnal desaturation is significantly high in moderate and severe COPD, however 3.3% mild COPD patients also had nocturnal desaturation most probably due to OSA
2. OSA incidence in patients with COPD is significant
3. 82.6% of COPD patients with OSA had high BMI and 17.3% had normal BMI
4. OSA is a major contributing factor in nocturnal hypoxemia in COPD patients.

Limitations of our study

Given the small number of sample size it is difficult to conclude regarding nocturnal desaturation in mild COPD. Association of OSA in many patients in our study contributes to nocturnal desaturation. Another study with a larger cohort of patients may help in identify nocturnal desaturation in COPD patients without OSA.

Acknowledgement

The authors thank Dr. D Y Patil Hospital and Research Center for giving this opportunity. This work was performed at Dr. D Y Patil Hospital and Research Center, Dr. D Y Patil University. Review and Writing occurred at DYPH and at the Department of Pulmonary and Sleep Medicine, Dr. D Y Patil Hospital.

REFERENCES

Ana C Krieger, NilamPatel, DanielGreen, FrankModersitzki MPH, IlanaBelitskaya-Levy, Angela Lorenzo, MichaelCutaia, 2007. Respiratory disturbance during sleep in COPD patients without daytime hypoxemia, *International Journal of COPD*, 2(4)

Block AJ, Boyson PG, Wynne JW. 1979. The origins of corpulmonale , a hypothesis. *Chest*, 75:109.

Calverley PMA, Brezinova V, Douglas NJ, Catterall JR, Flenley DC. 1982. The effect of oxygenation on sleep

quality in chronic bronchitis and emphysema. *Am Rev RespirDis*., 126: 206–210.

Calverley PMA, Brezinova V, Douglas NJ, *et al*. 1982. The effect of oxygenation on sleep quality in chronic bronchitis and emphysema. *Am Rev Respir Dis*., 126:206–10.

Catterall JR, Douglas NJ, Calverley PMA, *et al*. 1983. Transient hypoxaemia during sleep in chronic obstructive pulmonary disease is not a sleep apnea syndrome. *AmRev Respir Dis*., 128: 24–29.

Chaouat A, E. Weitzenblum, R. Kessler, C. Charpentier, M. Ehrhart, P. Levi-Valensi, J. Zielinski, L. Delaunois, R. Cornudella, J. Moutinho dos Santos, 1997. Sleep-related O2 desaturation and daytime pulmonary haemodynamics in COPD patients with mild hypoxaemia, *EurRespir J*., 10: 1730–1735

Clinical component for the home oxygen service in england and wales, BTS, January 2006

Croxton TL, Bailey WC. 2006. Long term oxygen treatment in chronic obstructive pulmonary disease: recommendations for future research. An NHLBI Workshop report. *Am J RespirCrit Care Med*., 174:373–8

Douglas NJ, Calverley PMA, Leggett RJE, Brash HM, Flenley DC, Brezinova V. 1979. Transient hypoxaemia during sleep in chronic bronchitis and emphysema. *Lancet*, i: 1–4.

Fleetham J, West P, Mezon B, Conway W, Roth T, Kryger MH. 1982. Sleep, arousals and oxygen desaturation in chronic obstructive pulmonary disease: the effect of oxygen therapy. *Am Rev Respir Dis*., 126: 429–433.

Flenly DC. 1978. Clinical hypoxia: causes, consequences & correction.(Lancet, 1:542-46).

Fletcher E.C., Miller J., Divine G.W. *et al*. (Nocturnal Oxyhaemoglobin Desaturation in COPD patients with arterial oxygen tensions above 60 mmHg) (*Journal—CHEST*, 1987/92/604-608)

Fletcher EC, GRAY BA, LEVIN DC. 1983. Nonapneic mechanisms of arterial oxygen saturation during rapid- eye –movement sleep. *J.Appl Physiol. – RespirEviron.Exer. Physiol*., 54:632-39.

Fletcher EC, Miller J, Divine GW, Fletcher JG, Miller T. 1987. Nocturnal oxyhemoglobin desaturation in COPD patients with arterial oxygen tension above 60 mmHg. *Chest*, 92: 604–608.

Fletcher EC. 1986. Sleep, breathing & oxyhaemoglobin saturation in chronic lung disease.In : Fletcher EC ,ed. Abnormalities of respiration during sleep: diagnosis, pathophysiology and treatment. Orlando, FL, Grune& Shatton, 155-79.

Flick MR, Block AJ. 1977. Continuous *in vivo* monitoring of arterial oxygenation in chronic obstructive lung disease. *Ann Intern Med*., 86: 725–730.

GOLD, The Global Strategy for Diagnosis, Management and Prevention of COPD (updated 2016)

Goldstein RS, Ramcharan V, Bowes G, *et al*. 1984. Effect of supplemental nocturnal oxygen on gas exchange in patients with severe obstructive lung disease. *N Engl J Med*., 310: 425–9.

Impact of CPAP Use and Age on Mortality in Patients with Combined COPD and Obstructive Sleep Apnea:The Overlap Syndrome Michael L. Stanchina, M.D.1; Lauren M. Welicky, M.D.1; Walter Donat, M.D.1; David Lee, M.D.1; 2015. Acute exacerbation of COPD in relation to overlap syndrome, Gothi, *et al.* Lung India • Vol 32 • Issue 6 • Nov – Dec.

Koo KW, Sax DS, Snider GL. 1975. Arterial blood gases and pH during sleep in chronic obstructive pulmonary disease. *Am J Med*., 58: 663–670.

Leitch AG, Clancy LJ, Leggett RJE, Tweeddale P, Dawson P, Evans JJ. 1976. Arterial blood gas tensions, hydrogen ion, and electroencephalogram during sleep in patients with chronic ventilatory failure. *Thorax*, 31: 730–735.

Levi-Valensi P, Weitzenblum E, Rida Z, *et al*. 1992. Sleeprelated oxygen desaturation and daytime pulmonary haemodynamics in COPD patients. *EurRespir J*., 5: 301–307.

Lewis C A, W Fergusson, T Eaton, I Zeng and J Kolbe doi, prevalence and impact on quality of life and Isolated nocturnal desaturation in COPD, THORAX10.1136/thx. 2007.088930

Littner MR, McGinty DJ, Arand DL. 1980. Determinants of oxygen desaturation in the course of ventilation during sleep in chronic obstructive pulmonary disease. *Am RevRespir Dis*., 122: 849–857.

Machado M, Vollmer VM, Bilderback AL, Oliveira MV, Leitao FS. 2010. CPAP and surviva lin moderate-to-severe obstructive sleep apnoea and hypoxaemic COPD. *EurRespir J*., 35:102-8.

Marin J, Soriano J, Carrizo S, Boldova A, Celli B. 2010. Outcomes in patients with chronic obstructive pulmonary disease and obstructive sleep apnea: the overlapsyndrome. *Am J RespirCrit Care Med*., 182:325-31.

McKeon JL, Murree-Allen K, Saunders NA. 1989. Supplemental oxygen and quality of sleep in patients with chronic obstructive lung disease. *Thorax*, 44:184–8.

Mulloy E, McNicholas WT. 1996. Ventilation and gas exchange during sleep and exercise in severe COPD. *Chest,* 109: 387–394.

Nattie EE, Barlett Jr D, 1978. Johnson K Pulmonary hypertension & Rt. Ventricular hypertrophy caused by intermittent hypoxia and hypercapnia in the rat. *Am Rev Respir Dis*., 118:653-58.

P.J.E. VOS, h.76 T.M. Folgering, C.L.A. Van Herwaarden, 1995. Predictors for nocturnal Hypoxaemia in COPD, *EurRespir J*., 8, 74–77, DOI: 10.1183/09031936.95.080 10074

Sampol G, Sagales MT, Roca A, de la Calzada MD, Bofill JM, Morell F. 1996. Nasal continuous positive airway pressure with supplemental oxygen in coexistent sleep apnoea-hypopnoea syndrome and severe chronic obstructive pulmonary disease. *Eur Respir J*., 9(1):111-116.

Sleep-related O_2 desaturation and daytime pulmonary haemodynamics in COPD patients with mild hypoxaemia, A. CHAOUAT *ET AL*., *EurRespir J*., 1997; 10: 1730–1735DOI: 10.1183/09031936.97.10081730

Trask CH, Cree EM. 1962. Oximeter studies on patients with chronic obstructive emphysema, awake and during sleep. *N Engl J Med*., 266: 639–642.

Wynne JW, Block AJ, Hemenway J, Hunt LA, Flick MR. 1979. Disordered breathing and oxygen desaturation during sleep in patients with chronic obstructive pulmonary disease. *Am J Med*, 66: 573–579.

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