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ORIGINAL ARTICLE

Possible Role of Non-Invasive Continuous Positive Pressure Ventilation in Patients with Overlap Syndrome: Obstructive Sleep Apnea and Chronic Obstructive Pulmonary Disease

Rabieh M.M. Hussein, Adel Attia A. Moussa, Reda M.A.Elghamry and Mohamed Taher Anwar*
Chest Diseases Department, Faculty of Medicine, Zagazig University.

***Corresponding author:**
Mohamed Taher Anwar
Chest Diseases Department, Faculty of Medicine, Zagazig University, Egypt.
Email:
dr_mohamedsurgeon@yahoo.com

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ABSTRACT

Background: Overlap syndrome (OS), describes the association and simultaneous presence of OSA and COPD, Overlap syndrome has poor clinical prognosis, including increased risk for cardiovascular morbidity, hospitalization due to COPD acute exacerbation, and all-cause mortality. Efficient CPAP treatment has been related to improved survival and decreased hospitalizations**.**

Methods: This study was carried out at sleep lab of Chest Department on 24 patients splitted into two groups Group 1: patients with overlap syndrome (OS) under medical treatment plus CPAP. Group 2: patients with (OS) under medical treatment only. All patients in the study were subjected to full medical history taking, Quality of sleep by Epworth sleepiness scale (ESS). Clinical examination; (general and local), Spirometry, complete lab investigation, polysomnography and Echocardiography.

Results: Statistically significant difference was observed between the two groups as regard AHI, nocturnal desaturation, mean pulmonary artery pressure, number of exacerbations per year and frequency of hospital admissions.

Conclusions: Patients with CPAP-treated overlap syndrome for a period of one year experienced improving in nocturnal desaturation, mean pulmonary artery pressure and number of exacerbations.

Keywords: Apnea/hypopnea index; Overlap Syndrome; Mean pulmonary artery pressure; Nocturnal desaturations; Exacerbations

INTRODUCTION

Both COPD and OSA are highly prevalent, suggesting that both disorders that occur together (overlap syndrome) are likely to be widespread based solely on chance association. Both COPD and OSA have related to hypoxia and systemic inflammation, which lead to cardiovascular and other comorbidities, and high prevalence of pulmonary hypertension in overlap syndrome patients [1].

There are several factors which that affect the relationship between COPD and OSAS. Body mass and smoking may affect relationships with the pathophysiology. Neck obesity leads to narrowing of the upper airways, truncal obesity encourages ventilatory disruption through reduced compliance with the chest wall and respiratory muscle strength, and is also associated with reduced FRC, which leads to mismatching ventilation-perfusion [2]. A complex relationship between hypoxemia, inflammatory mediators and high sympathetic activity was suggested to explain the high risk of death and exacerbation of COPD relative to a COPD population only. Overlap syndrome patients show more extreme desaturation of oxygen during sleep and experience a higher rate of respiratory insufficiency than patients with OSA only [3].

CPAP remains the approved standard treatment for OSA, and is also the standard recommended for overlap syndrome [4]. Fixing repeated collapse of the airway can improve pulmonary function [5], Others postulated that discharging the respiratory muscles could decrease the production of hypoventilation, oxygen or carbon dioxide from the respiratory muscles. Both muscles can be protected by CPAP, as it avoids the increased resistance of the upper airway during sleep. Alternatively, in severely COPD, CPAP can offset intrinsic PEEP [6].

CPAP therapy is effective in improving RDI, nocturnal hypoxemia, hypercapnia and daytime sleepiness. In Overlap syndrome patients, CPAP can benefit from improved respiratory mechanics, such as reduced breathing work by minimizing hyperinflation [7,8].

METHODS

Written informed consent was obtained from all participants, the study was approved by the research ethical committee of Faculty of Medicine, Zagazig University. The study was done according to The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

This study was carried out at sleep lab of Chest Department, Zagazig University Hospitals, for 12-months period from January 2018 to January 2019. on 24 patients was included in the study divided into two groups (12 patients in each group):

Group 1: patients with overlap syndrome (OS) under medical treatment plus CPAP.

Group 2: patients with OS under medical treatment only.

All patients received a pharmacological treatment according to the diagnostic and treatment standards of COPD patients (GOLD 2017) [9].

Inclusion Criteria:

Patients were enrolled according to the following criteria in the study:

Stable COPD: mild (GOLD 1) and moderate (GOLD 2) Patients was diagnosed according to **(GOLD 2017**) [9]. Patients had been at least 4 weeks free from acute exacerbations.

All patients reported sleep disordered breathing symptoms: The Epworth sleepiness scale (ESS) was used to assess excessive daytime sleepiness.

Exclusion criteria:

Stable COPD patients with PaO2 < 60 mmHg or severe (GOLD3) and very severe COPD (GOLD 4). Patients with gas exchange derangements were excluded because of any other causes.

Concurrent anxiolytic or analeptic treatment and other chronic non-respiratory conditions associated with it.

Overlap syndrome patients who started treatment with CPAP but who showed <3 h per night compliance.

All patients in the study were subjected to the following:

Informed written consent will be taken from all participants of the study, Full medical history taking and history of sleep duration and quality by ESS, **history** of associated comorbidities, **clinical examination:** full clinical examination including general , local and ENT examination, **assessment of obesity:** Body mass index **(BMI)** [10] and Neck Girth circumference **(NC)** [11], **plain x-ray chest (Postero-anterior and lateral views), spirometry:** Forced vital capacity (FVC) percentage of predicted, forced expiratory volume in the first second (FEV_1) percentage of predicted), FEV_1/FVC% post bronchodilator and FEV_1 reversibility < 12 % at 0 month and at the end of the study using THOR SOFT SPIRO-TUBE [9], **arterial blood gases analysis (ABGs)**.were measured at 0 month and after 12 months of the study, **laboratory investigations:** Complete blood count (CBC).,Liver function tests (LFT) , tests for Kidney function (KFT), Random blood sugar ,Thyroid function tests (TSH, T3, and T4),**color Doppler echocardiography:** Before and after the end of the study (0-12 months). Measures resting daytime mean PAP (the subcostal approach was used. The mean value of three measurements was considered at 0 month and 12 months [12], **Polysomnography for assessment of Sleep Quality:** A full-night polysomnographic sleep study was done using (SOMNO screen™ plus which is manufactured in Germany) to all patients.

Data collection, processing:

Data were collected manually according to variables of the study mentioned above in a hard data sheet, and then data entry was made according to a unified code.

Statistical analysis

Data were collected, tabulated and analyzed by SPSS 20, software for Windows. The level of significance was set at $P < 0.05$.

RESULTS

Table (1) demonstrates no significant difference between the two groups as regard age, sex, smoking status, also the two groups matched. (P value > 0.05).

Table (2) reveals there was statistically significant difference as regard Sleep latency, N1, N2, N3, REM stages, AHI, RDI, Number of desaturations, minimum SPO2 and maximum heart rate between the two groups after 1 year of the study. (P value < 0.05).

Table (3) shows there was statistically significant improvement of spirometric parameters in group I after one year of using CPAP as regard FEV1/ FVC %, FEV1% predicted and FVC % (P value < 0.05).

Table (4) shows there was no significant difference in mean pulmonary artery pressure between the two

groups at 0 month of the study with (P value > 0.05).

While after one year There was highly statistically significant difference between the two groups (P value < 0.01). As regard change assessment group I significantly decrease in mean pulmonary artery pressure with highly statistically significant difference (P value < 0.01).

Table (5) shows that Group I was significantly lower at number of exacerbations with statistically significant difference between the two groups after one year of the study (P value < 0.05).

Table (6) shows statistically significant difference in frequency of hospital admission per year in group I that was less after one year from starting CPAP (P value < 0.05).

Table (1): Demographic data of the studied patients:

			Group I	Group II	t/ X^2	P
Age yrs (Mean ±SD)			55.41 ± 6.99	56.83 ± 6.13	0.52	0.621
Sex	**Female**	**N (%)**	5 (41.7 %)	7 (58.3 %)	0.151	0.92
	Male	**N (%)**	7 (58.3 %)	5 (41.7 %)		
Smoking	**Smoker**	**N (%)**	5 (41.7%)	6 (50 %)	0.16	0.68
	Non	**N (%)**	7 (58.3%)	6 (50 %)		
	Pack year	**Mean ±SD**	18.91 ± 23.76	25.75 ± 27.23		
Total		**N**	12	12		
		%	100.0%	100.0%		

Table (2): Polysomnographic parameters distribution of the studied patients after CPAP and medical ttt for group I and medical ttt for group Π (after 1 year):

	Group I	Group II	t	P
Sleep efficiency %	84.01± 5.71	80.79± 7.06	0.841	0.231
Sleep latency	7.93± 18.35	18.80± 19.80	-4.854	0.00**
N1 %	12.45± 4.09	76.21± 21.84	-25.632	0.00**
N2 %	45.53 ± 7.91	8.54 ± 7.53	31.325	0.00**
N 3 %	17.15 ± 4.44	2.37 ± 2.38	16.745	0.00**
REM %	24.03± 21.73	10.81± 13.31	20.587	0.00**
AHI /h	4.9± 2.2	52.05± 21.54	-28.632	0.00**
RDI /h	5.34± 1.9	53.67± 22.57	-31.254	0.00**
Base SpO_2 %	92 ± 3.08	90.08± 1.43	0.571	0.511
Minimal SpO_2 %	72.22± 3.57	62.41± 3.25	2.273	0.035*
Number of desat.	12.78± 31.15	59.36± 23.10	-28.321	0.00**
Max HR / minute	122.16 ± 27.12	160.91 ± 10.35	3.492	0.002*
Min HR /minute	62.58± 3.50	60.38± 4.47	1.521	0.095

Table (3): Spirometric parameters distribution between the studied groups at (0 month) and after (1 year) of the study:

Group / Spirometry		Group I	Group II	t	P
0 month	**FEV_1/ FVC %**	59.66 ± 4.55	58.75 ± 4.11	1.35	0.22
	FEV_1 % pred.	61.25± 10.38	61.50 ± 6.77	-0.07	0.94

Group		Group I	Group II	t	P
Spirometry					
1 year	FVC % pred	79.08± 4.54	80.83 ± 3.78	-1.02	0.31
	FEV_1/ FVC %	61± 4.51	58.33 ± 4.07	1.481	0.153
	FEV_1 % pred.	62.33±10.61	60.5 ± 7	0.545	0.592
	FVC % pred.	81.08±2.96	80.33 ± 2.57	1.684	0.106
P1		0.001**	0.125		
P2		0.025*	0.085		
P3		0.011*	0.624		

Table (4): Mean pulmonary artery pressure (mmHg) distribution between the two groups at (0 month) and after (1 year) of the study:

	Group I	Group II	t	P
0 month	33.0±5.0	32.75±3.59	0.140	0.890
1 year	23.0±2.4	32.66±2.96	-8.655	0.00**
P	0.00**	0.59		

Table (5): Number of Exacerbation per Year distribution between the two groups after (1 year) of the study:

		Group I	Group II	X^2	P
0	N	8	1	10.84	0.004*
	%	66.7 %	8.3 %		
one	N	4	6		
	%	33.3 %	50 %		
≥ 2	N	0	5		
	%	0.0%	41.7 %		
Total	N	12	12		
	%	100 %	100 %		

Table (6): Frequency of hospital admission Per Year among the studied group I at (0 month) and after (1 year) of the study:

		0 month	After 1 year	X^2	P
0	N	4	11	8.933	0.011
	%	33.3%	91.7%		
once	N	5	1		
	%	41.7%	8.3%		
twice	N	3	0		
	%	25 %	0.00%		
Total	N	12	12		
	%	100 %	100 %		

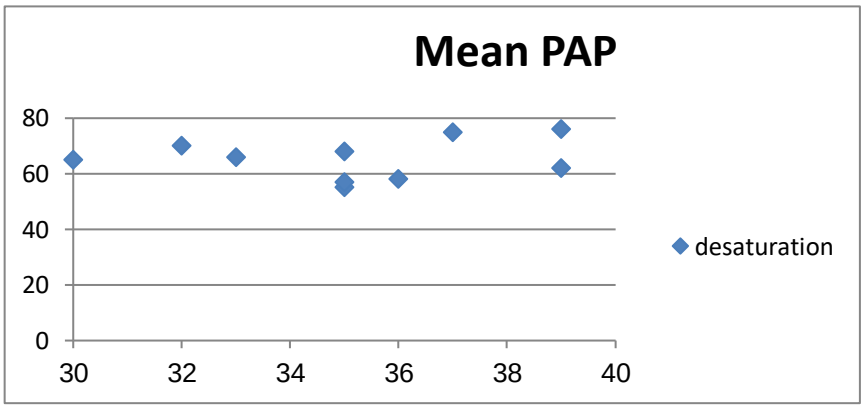

Figure (1): scattered plots show positive correlation between mean pulmonary artery pressure and number of desaturations

DISCUSSION

Several studies assessed the impact of CPAP on overlap syndrome; this study was designed to detect the possible role of continuous non-invasive ventilation in overlap syndrome. This study was conducted on 24 patients of overlap syndrome divided into two groups (12 patients in each group): Group 1 (group with CPAP) under medical treatment and CPAP and Group 2 (group without CPAP) under medical treatment only for 12-month period.

In this study as regard the polysomnographic parameters of studied patients, there was abnormal sleep architecture in both groups before CPAP but after CPAP there was significant improvement in sleep architecture in group with CPAP (table 2). That was in harmony with that of Philippe et al., who found that However, CPAP treatment did not affect sleep quality or overall sleep time, but substantially improved the sleep architecture by reducing the proportion of stage 1 sleep and increasing slow-wave sleep as well as REM stage sleep CPAP treatment, also significantly increased the minimal SaO2 and the time spent with SpO2 < 90 % in studied patients [13]. Also, Lacedonia et al., found that overlap syndrome patients had a lower level of diurnal PaO2 and Night-time use of CPAP can increase diurnal PaO2 not only in patients with overlap syndrome but also in patients with OSAS [14]. Sampol et al, proved that night-time CPAP could boost oxygenation overnight in patients with overlap syndrome [15].

Regarding spirometric parameters of studied patients; group with CPAP significantly improved as regard FEV1/ FVC %, FEV1% predicted and FVC % but group without CPAP didn't significantly change (table 3), this result was in harmony with De Miguel et al., who assessed the effects of CPAP treatment on lung function in overlap syndrome patients over two consecutive years. There were statistically significant increases in PaO2, FEV1% pred., and forced vital capacity % after 6 months of CPAP therapy [7]. Also, Mansfield and Naughton, evaluated the outcome of CPAP on lung function in COPD and sleep disordered breathing patients, they found significant improvement in patients FEV1% pred. [16]. These findings can be clarified by different mechanisms, according to De Miguel et al., such as bronchodilation, decrease in respiratory load, improvement of ventilation/perfusion ratio [7]. On the other hand, Sampol et al., note improvement in arterial blood gases, but lung function tests have not been improved, that is may be due to different sample size and improvement in arterial blood gases was an acute result but longer-term effects of CPAP on lung functions were not studied [15]. Also, ÕBrien and Whitman, recorded a significant decline in FEV1% pred. and FVC % in overlap syndrome patients who used CPAP for more than 4 hours/day relative to non-compliant patients. However, this result may be due to the patients who enrolled in their study were moderate and severe COPD while in this study the patients were mild and moderate COPD, time of their study was 4 years 2 years retrospective and patients followed for another 2 years [17].

By highlighting the mean pressure of pulmonary artery at the start of the study and after one year this study observed that most of patients had increase in mean pressure of pulmonary artery at the start of the study, but after one year of the study the mean pulmonary artery pressure significantly decreases in group 1 while other group show no significantly

change in mean pulmonary artery pressure (table 4). This result was in line with Sanner et al., In 20 per cent of OSAS patients without lung disease, PH was found [18]. Also, Schäfer et al., who noted that systolic PAP increased to 39 ± 16 mm Hg (end of apnea) from 28 ± 12 mm Hg (beginning of apnea); [19]. Also, Hawrylkiewicz et al., studied Seventeen patients with OS in whom Pulmonary artery catheterization revealed, elevated mean PAP and PVR, and normal PW and CO. pulmonary arterial pressure was normal in three patients, mean 12±3 mmHg. Highly statistically significant difference was found in 14 patients with pulmonary hypertension (mean PAP = 27 ±5 mmHg) [20]. Toraldo et al., who also found that a decrease of 30% in mPAP after using CPAP after 1st 6 months in 24 months follow-up study [21]. Also, several studies noted improvements in pulmonary hemodynamics after initiation of CPAP therapy in overlap syndrome patients, Sajkov et al., And Arias et al., that had found a significant fall in PAP after 3 to 6 months of nocturnal CPAP treatment [22, 23]. SAJKOV et al., explained potential reason for Decrease in pulmonary artery pressure with CPAP Treatment may be due to Decrease in pulmonary vascular reactivity to hypoxia enhanced endothelial pulmonary function, known for regulation of pulmonary vascular tone [22].

By showing of number of exacerbations and frequency of hospital admissions between studied patients at the start of the study and after one year there were significant improvement in number of exacerbations and times of hospital admissions in group 1 due to exacerbations after one year (table 5, 6). This was in accordance with that of Marin et al., who reported a beneficial effect of CPAP in minimizing COPD exacerbations in COPD patients and associated OSA, a disparity in the initial extreme COPD exacerbation in CPAP-treated patients relative to untreated Overlap syndrome patients during follow-up. Patients diagnosed with NIV after 2 years of follow-up had less hospital days per patient per year [24]. Also, Peker et al., found that treatment of OSA with CPAP may reduce the need for acute cardiovascular and pulmonary hospital admission [25]. Also, Singh et al., who investigated Impact of CPAP treatment on hospitalization rates in Overlap syndrome patients reported that Initiation of CPAP therapy in overlap syndrome patients was associated with significant decrease in hospitalization rates for COPD-related conditions in the one-year post initiation of CPAP therapy and explained that was due to reduction in hypoxemia and inflammation after initiation of CPAP therapy [26]. In contrast to this study ÕBrien and Whitman, observed an increase in the number of exacerbations following the implementation of CPAP therapy, this change was not statistically significant [17].

A positive correlation, in this study, between the number of desaturations and mean pulmonary artery pressure was evident that was statistically significant (graph 1). That was in agreement with Hawrylkiewicz et al., that found there were negative correlations between SaO2 and mean pulmonary artery pressure were found but there was no correlation between AHI and mean pulmonary artery pressure [20].

CONCLUSIONS

Overlap syndrome patients CPAP-treated besides the recommended pharmacological drugs for a period of one year experienced: Significant improvement of nocturnal desaturations, Significant improvement in spirometric parameters, Significant decrease in number of exacerbations per year and frequency of hospitalization and Significant improvement in mean pulmonary artery pressure levels.

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