

Association Between Chronic Obstructive Pulmonary Disease and Sleep Apnea - *Overlap Syndrome*- Experience of Pulmonology Clinic Tg. Mures, Romania

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Association between chronic obstructive pulmonary disease (COPD) and sleep apnea SA (overlap syndrome - OS) includes serious clinical manifestations and high mortality due to early respiratory failure, cardiovascular and metabolic complications from both diseases. 90 COPD patients (85.5% males) were strongly suspected to have concomitant SA after clinical examination and sleep questionnaires. We performed a cardioventilatory poligraphy during sleep. 82 patients (91.1%) from our OS group had obstructive sleep apnea (OSA), 8 patients (8.9%) mixed apnea and 20% had also OHS. 17 (18.8%) of OS were overweight and 66 (73.3%) obese. A third of them were in a very active group of age: 49 patients (54.4%) under 60 year-old and 11 patients (12.2%) between 61-65 year-old. We noted severe complication/comorbidities in our OS group: 63.3% hypertension, 43.3% core pulmonale, 31.1% arrhythmia, 32.2% cardiac failure, 38.8% dyslipidemia, 31.1% diabetes. The second night investigation permitted titration for the targeted pressures for CPAP therapy (Continuous Positive Airways Pressure). Treatment of OS patients had an interdisciplinary approach: CPAP in OSA, BPAP (Bi-level Positive Airways Pressure) in OHS, inhaled bronchodilators, treatment of cardiovascular comorbidities, pulmonary rehabilitation, weight loss, tobacco/alcohol cessation counseling, and oxygen therapy in remaining hypoxemic patients. 51.2% of patients had not accessibility for long time CPAP (lack of coverage by the public health system). OS included clinical aspects of severity due to both COPD and OSA. Clinical investigation, sleep questionnaires, assessment of the diurnal somnolence and sleep cardiorespiratory poligraphy are recommended in all COPD patients. Obesity was the main risk factor for OSA in COPD patients.

Keywords: COPD, obstructive sleep apnea, obesity, overlap syndrome

Association in the same patient of the sleep apnea (SA) with other respiratory diseases (chronic obstructive pulmonary disease - COPD, asthma, bronchiectasis, cystic fibrosis or diffuse fibrosis) is called *overlap syndrome* (OS) [1-3]. The best studied is the association SA with COPD. OS has a high prevalence in the population linked to the high prevalence of both diseases. However the two diseases have some risk conditions like smoking, environmental exposure, obesity, advanced age. COPD is still the fourth leading cause of death worldwide and, considering the high diseases prevalence and complication, it will become the 3rd leading cause of death by 2020 [4].

The COPD prevalence is estimated at about 10% from general population [5]. COPD alone associates various sleep disorders and respiratory sleep disorders: insomnia, frequent awakenings (by cough, obstruction, and wheezing, adverse effects of medication), nocturnal hypoxemic episodes (by hypoventilation and anomalies in V/Q ratio) and an increased risk of cardiovascular and metabolic complications [6-9].

On the other hand SAS is an independent risk factor for cardiovascular, metabolic disorders and for neuropsychological impairment [10,11]. Thereby OS will include aspects of clinical severity and severe prognosis

due to respiratory complications, cardiovascular and metabolic complications from the both diseases and an increased risk of mortality. OS include accentuated daytime sleepiness, more severe nocturnal oxygen desaturation and daytime hypercapnia than in each disease alone [12]. OS progresses faster to pulmonary hypertension and core pulmonale than COPD alone [13-15]. Patients with OS have more frequent cardiac arrhythmias caused by dramatic desaturation [16].

Several studies on OS have indicated a high prevalence of SA in COPD patients [17,18]. We conducted a study to analyze the presence of SA in COPD patients in our Clinic and the particularities of the overlap syndrome OS (COPD and Obstructive Sleep Apnea) hospitalized in our Pulmonology Clinic.

Experimental part

We studied directly the clinical features and investigation tests in 175 COPD hospitalized patients in the Pulmonology Clinic Tg. Mures (during 8 month). We analyzed symptoms and signs of the underlying disease (COPD) but also association with sleep apnea SA, cardiovascular and metabolic complication and carried out investigation. We used sleep questionnaire evaluation of diurnal somnolence and nocturnal symptoms in COPD patients (Epworth, Berlin

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questionnaires), smoking, presence of obesity, prevalence of the disease by gender, alcohol consumption. We divided the patients into 2 COPD groups (COPD with and without SA) and we made some comparisons between 2 groups and with data from literature.

Results and discussions

The study group comprising 175 patients COPD was strongly suspected to have concomitant SA after clinical examination, sleep questionnaires and cardio-ventilatory polygraphy during sleep. 90 (51.4%) COPD patients with high suspicion of SA were confirmed to have also SA or association between SA and obesity - hypoventilation syndrome (OHS). We compare our group of OS with the control group that included 85 COPD patients without SA or OHS. In all patients we ameliorated other causes for poor sleep (dyspnea, insomnia by anxiety and we did not use in the second part of the day and in the evening systemic glucocorticoids, or teofilin to exclude the possible side effects of medications).

82 patients (91.1%) from our OS group had obstructive sleep apnea (OSA), 8 patients (8.9%) mixed apnea and 20% of the entire group had also OHS. 17 (18.8%) of OS were overweight and 66 (73.3%) obese.

The patients were part of all age groups but a third of them were in a very active group of age: 49 patients (54.4%) under 60 year-old and 11 patients (12.2%) between 61 and 65 year-old.

77 patients (85.5%) were males and 86.6% from the entire group were smokers (active or former smokers - more than 15 packs-year). The patient from 2 groups had similar demographic characteristics but differences between the smoking status, BMI and comorbidities (fig. 1).

We notice significant differences in severity and prevalence of comorbidities/complications between two groups of COPD patients. In the OS group arterial hypertension was more frequent with 22.2%, core pulmonale with 15.1%, diabetes with 13.5%, left ventricular failure and global cardiac failure with 10%. 11.1% with OS vs 3.5% with COPD alone needed transfer in ICU ward for more complex treatment: noninvasive mechanical ventilation NIMV (7 patients) and 3 patients for endotracheal intubation for hypercapnic encephalopathy.

The second night investigation (fig. 2 and 3) permitted titration for the targeted pressures inside of therapy with CPAP (Continuous Positive Airways Pressure). Treatment

COPD total group	Study group COPD plus SA or OHS (OS)	Control group (COPD without SA or OHS)
Number or patients	90	85
Males	77 (85.5%)	68 (80%)
Smoking	78 (86.6)	62 (72.9%)
COPD grade of risk severity	Group B - 23 (25.55%) Group C - 26 (28.88%) Group D - 41 (45.55%)	Group B - 21 (24.7%) Group C - 25 (29.4%) Group D - 39 (45.8%)
BMI	Underweight 2 (2.2%) Normal weight 4 (4.4%) Overweight 35 (38.8%) Obesity 49 (54.4%)	Underweight 25 (29.4%) Normal weight 2 (2.3%) Overweight 35 (41.1) Obesity 23 (27%)
Complication/comorbidities	<ul style="list-style-type: none"> Hypertension 57 (63.3%) Core pulmonale 39 (43.3%) Arrhythmia 28 (31.1%) Cardiac failure 29 (32.2%) Dyslipidemia 35 (38.8%) Diabetes 28 (31.1%) 	<ul style="list-style-type: none"> Hypertension 35 (41.1%) Core pulmonale 24 (28.2%) Arrhythmia 20 (23.5%) Cardiac failure 19 (22.3%) Dyslipidemia 34 (40.0%) Diabetes 15 (17.6%)
Hypercapnic pts with ICU transfer for MV	10 (11.1%)	3 (3.5%)

Fig. 1. Characteristic of the 2 group of COPD patients (Group of patients with OS) and control group

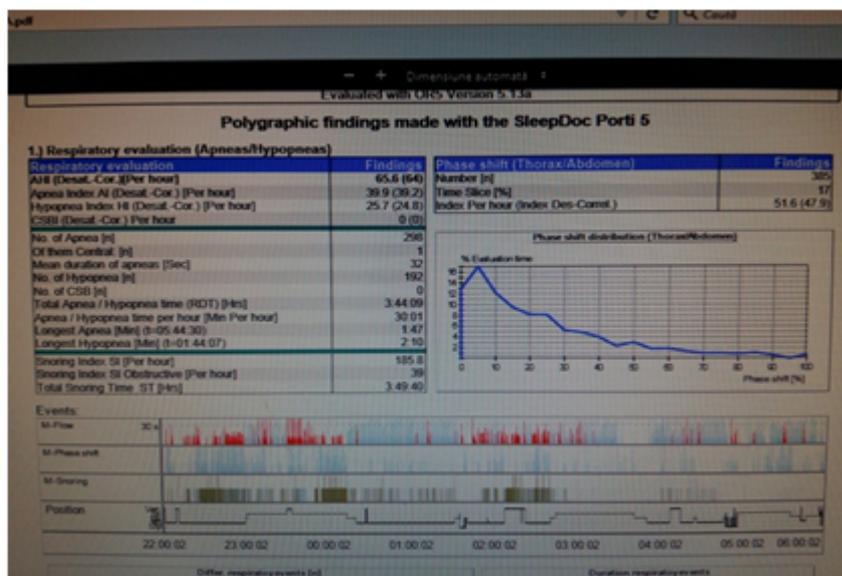


Fig. 2. Polygraphic report - Severe obstructive sleep apnea (with AHI - apnea hypopnea index 65.6/hour)

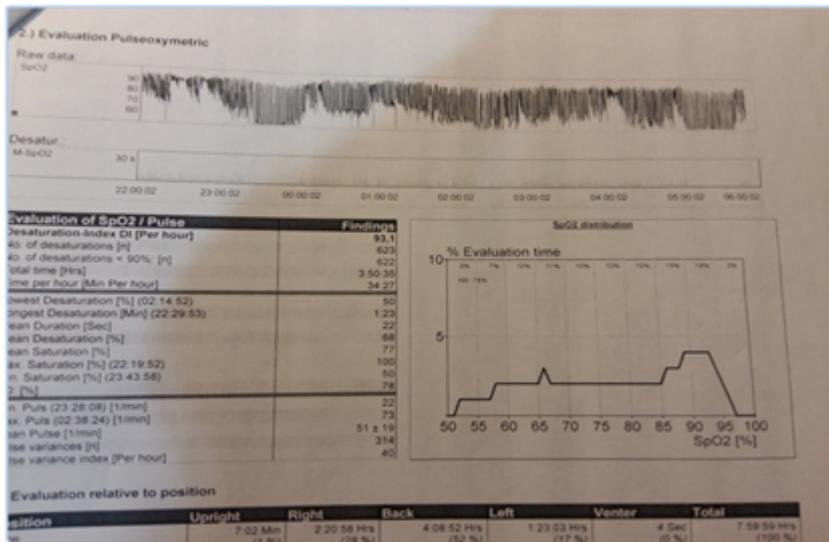


Fig. 3. Desaturation index extremely severe 93.1events/hour with 78% of total sleep time spent at a saturation under 90% (with very severe desaturation)

of OS patients had an interdisciplinary approach: CPAP in OSA, BPAP (Bi-level Positive Airways Pressure) in OHS, inhaled bronchodilators, treatment of cardiovascular comorbidities, pulmonary rehabilitation, weight loss recommendation, tobacco/alcohol cessation counseling, and oxygen therapy in remaining hypoxemic patients. 51.2% of patients had not accessibility for long time CPAP (lack of coverage by the public health system).

We have chosen the COPD patients that presented diurnal somnolence, poor quality of sleep, frequent arousals and association of risk factors for SA [19-21]. However it is known that patients with COPD have sleep disorders by several causes besides SA [22]. So we did not consider patients with nocturnal cough interfering with sleep, insomnia by dyspnea or anxiety and we did not use medication that could interfere with sleep.

Our study analyzed the difference between COPD alone and COPD associated with sleep apnea. The notable risk factor in our study was obesity 54% versus 27% in COPD alone [19]. Obesity was the cause also for the OHS (20%). In the same time obesity is an independent risk factor for cardiovascular disease especially in women [21].

The great percentage of cardiovascular complication in OS could be better understand if we think about it him OS there is a triple cumulative cardiovascular risk (by obesity, COPD itself and by sleep apnea) [19-21].

Smoking was more prevalent in the OS group (86.6%) but was extremely frequent also in the group with COPD alone (72.9) comparing with the country average in general population (26%). Smoking was in our group the main risk factor for COPD like the literature described [22], but it was an independent risk factor also for cardiovascular disease and SA (by sustained inflammation at the superior airways) [23]. Taking into account the he ones above smoking control has to be a permanent necessity through a sustained early education in general population before the occurrence of the described disorders.

Treatment of the OS depended of the severity of the disease and the levels of needed pressure at the titration and the presence of the OHS and also after 18 cmH2O we indicated bi-level CPAP). Bi-level have benefits over CPAP among severe COPD patients where it may aid with nocturnal ventilation and resting of respiratory muscles [24].

Because of the seriousness of the association of diseases, the early detection of each disease is necessary. Sleep studies may be strongly recommended in COPD especially in obese patients, snoring patients or in those who present symptoms compatible with SA (headache,

diurnal somnolence, uncomfortable sleep with frequent arousal, severe cardiovascular or metabolic comorbidities, cognitive decline) [2,6,12].

In the same time associated SA will be suspected in COPD with modest obstruction but with great nocturnal hypoxemia, polycythemia, core pulmonale or early cognitive decline. Therefore all patients with SA will be investigated by pulmonary function tests. Given the severe complications, OS requires complex treatment (for both diseases) combined bronchodilator or triple therapy (anticholinergic, beta2 agonists and corticoids) in COPD, and SA correction by permanent CPAP/biPAP treatment. Oxygen therapy could be necessary in remaining hypoxemic patients [7,24]. Pulmonary rehabilitation, lifestyle changes and weight loss are parts of the complex therapy in OS [25].

Conclusions

Overlap syndrome (COPD and sleep apnea) included clinical aspects of severity due to both COPD and SA. Clinical investigation by questionnaires of the diurnal somnolence and sleep cardiorespiratory poligraphy are recommended in all COPD patients for an early diagnosis of the associated SA disease and targeted treatment. Obesity was the main risk factor for OSA in COPD patients. Smoking was more prevalent in the OS group. Fighting against risk factor in OS (obesity, smoking, environmental exposure) is part of the complex treatment of these patients that contribute to the prognostic improvement.

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