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Research Article

Prognostic factors in evolution of sleep apnea

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Abstract. Objective: Obstructive sleep apnea (OSA) represents a highly prevalent pathology that, left untreated, can cause important complications. Continuous positive airway pressure (CPAP) represent the gold standard for treatment of OSA. The aim was to study the improvement of polygraphy indexes after CPAP and to evaluate the influence of comorbidities on the severity of OSA. Material and method: This is a prospective, observational, longitudinal, analytic, cohort study. Of the 150 patients from the study group, 93 patients with OSA were included, aged 60 (58;64) years, sex ratio female/male 1:4. Patients have performed respiratory polygraphy examination in 3 different steps: at the time of diagnosis, during titration and at three months checkup, after treatment with CPAP. Results: Most of patients included in the study are male, urban residence, obese grade I or III, with NYHA class II of heart failure, suffer from stage 2 arterial hypertension, dyslipidemia, consume coffee and have severe sleep apnea. There has been a considerable improvement in all respiratory parameters right after titration and an even greater improvement was observed during the three months control after CPAP therapy ($p<0.001$). Epworth Sleepiness Scale significantly decreased by comparing the starting point with the 3-monthscheckup ($p<0.001$).Sleep apnea severity was correlated with obesity ($r=0.269$; $p=0.009$). In women, sleep apnea severity (AHI) was correlated with BMI ($r=0.592$; $p=0.005$), age ($r=0.516$; $p=0.01$), and neck circumference ($r=0.584$; $p=0.005$). Apnea hypopnea index (AHI) ($p=0.005$), Epworth Sleepiness Scale ($p=0.04$) and the total number of respiratory events ($p=0.009$) decreased more in patients without arterial hypertension compared to those with hypertension. Also, AHI decreased more in patients without heart failure then in those with it ($p=0.05$). No relationship was found between sleep apnea and smoking or alcohol consumptionat the 3 months control. Conclusion: Sleep apnea patients associated multiple comorbidities. All respiratory parameters and Epworth scale, significantly improved after three months of CPAP therapy.

Key Words: sleep apnea, respiratory polygraphy, continuous positive airway pressure.

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Introduction

Worldwide, prevalence of obstructive sleep apnea (OSA) increases significantly and data suggest that 14% - 49% of middle-aged men have clinically significant sleep apnea (Garvey et al 2015). If untreated, serious complications may occur.

Acute adverse consequences are determined by the occurrence of systemic hypoxia and hypercapnia, the increase in negative intrathoracic pressure and repeated awakenings through the night. Chronic effects of untreated OSA are represented by disruption of the autonomic nervous system, activation of inflammation and oxidative stress with pro-atherogenic effects, vascular and endothelial dysfunction and the onset of metabolic disorders. This pathology condition include effects like: cardiac arrhythmia, heart failure, high blood pressure, myocardial ischemia, pulmonary hypertension, stroke (Somers et al 2008), type II diabetes, depression, anxiety.

Continuous positive airway pressure (CPAP) represents the gold standard treatment of OSA(Batool-Anwar et al 2016). Treatment with continuous positive airway pressure abolishes episodes of OSA and also reduces sympathetic activity (Shivalkar al 2006). This decreases daytime sleepiness, augments cognitive function and improves the quality of life (Wons et al 2015). A minimum of 3 to 4 hours of treatment with CPAP each night is needed to achieve long-term benefits (Leger et al 2016).

The aim was to study the improvement of polygraphy indexes after CPAP and to evaluate the influence of comorbidities on the severity of OSA.

Material and Method

This is a prospective, longitudinal, observational, analytic, cohort study. From January 2014 to August 2014 at 'Leon Daniello' Clinical Hospital of Pulmonology in Cluj-Napoca, all patients with suspicion of OSA who addressed to the clinic, were included. 150 patients formed the study group, of which 123 men and 27 women, aged between 19 to 78 years. The patients who fulfilled the following inclusion criteria, they were taken into the study: patients agreed and signed the informed consent, underwent all the investigations, were diagnosed with OSA by respiratory polygraphy, stick to the treatment (at least 4 CPAP hours/night), turn back for control and examination after 3 months. Exclusion criteria were: lack of informed consent; study abandonment; refusal to undergo treatment; cardiac or pulmonary severe disease; heart failure NYHA IV (New York

Heart Association). After going to inclusion and exclusion criteria, 93 patients were eligible for the study.

The approval of the University of Medicine and Pharmacy "Iuliu Hatieganu" Cluj –Napoca, of the ethics committee and the informed consent of each patient were obtained.

Demographic data (age, gender, environment urban or rural), social data, clinical data (body mass index (BMI), abdominal and neck circumference, blood pressure and pulse rate) were gathered. Detailed patient medical history was conducted and aspects related to hypertension, type 2 diabetes, dyslipidemia, category of congestive heart failure based on NYHA classification, toxic working environment and consumption of toxic: alcohol, coffee, tobacco, medication, sleep position, were noted. The diagnosis was established based on medical history and a specific questionnaire –the Epworth Sleepiness Scale (Johns et al 1993), which was completed by all patients. Depending on each response, certain score was given. A total score ≥ 10 indicated mild sleepiness and a total score ≥ 18 indicated severe daytime sleepiness.

Patients were subjected for 7 hours to respiratory polygraphy examination (between 11 pm- 6 am). All patients with an apnea-hypopnea index (AHI) > 5 were included in the study. They were divided based on severity of the sleep disorder into: mild (AHI between 5-15 per hour) or moderate (AHI between 15-30 per hour) or severe (AHI > 30 per hour) sleep apnea.

The examinations performed were: biological samples (blood count, lipid profile, blood sugar); chest X-ray; spirometry; electrocardiogram; echocardiography; otorhinolaryngology (ENT) examination. Of the 92 patients, 6 neededalso surgery in the ENT field, and the remaining patients underwent only CPAP therapy.

The NOX T3 portable sleep monitor device was used in the study. The parameters observed were: AHI, the total number of respiratory events (apnea and hypopnea events), minimum oxygen saturation, average oxygen saturation, the longest apnea and oxygen desaturation index/h (ODI). Echocardiography was done using the Acuson X 300 Siemens device. The parameters observed were: left ventricle, interventricular septum, posterior wall, left atrium, right ventricle; ejection fraction; diastolic function; kinetic disorders; valvular heart disease; pulmonary hypertension and pericardial effusion.

After being diagnosed with OSA, patients followed individualized treatment. After three months, patients returned for checkup: they completed a new Epworth sleepiness scale form and underwent sleep respiratory polygraphy recording. One year after the diagnosis and initiation of treatment, all patients were contacted by phone and it was noted whether or not they continued treatment with CPAP.

Statistical analysis was achieved using MedCalcStatistical Software, the 16.8 version (MedCalc Software bvba, Ostend, Belgium; https://www.medcalc.org; 2016). The quantitative data were represented as median and 25th - 75th percentiles (non-normal distribution) and the qualitative data as frequency and percentage. The difference between two repeated measurements was checked with the Wilcoxon signed-rank test. The association between two continuous variables was assessed using the Spearman rho coefficient. A p value <0.05 was considered statistically significant.

Results

Table 1 describes the general characteristics of the study group. Of the 150 patients included in the study, 93 have met the inclusion and the exclusion criteria. Most of them are male, urban residence, obese grade I or III, with NYHA class II of heart failure, suffer from stage 2 arterial hypertension, dyslipidemia, consume coffee and have severe sleep apnea.

Table 1. The general characteristics of the study group

Variable	Value
Age (years)	60 (52;64)
Men n(%)	72 (77.4%)
Urban residence n(%)	81(87.1%)
Body mass index (kg/m^2)	34 (30.25;38)
Waist circumference (mm)	123 (112;130)
Neck circumference (mm)	44 (42;46)
Obesity	
- Overweight n(%)	13 (13.9%)
- grade I n(%)	28 (30.1%)
- grade II n(%)	16 (17.2%)
- grade IIIn(%)	28 (30.1%)
Epworth Sleepiness Scale	11 (7.5;15)
Sleep apnea	
- mild form n(%)	14 (15.0%)
- moderate form n(%)	23 (24.7%)
- severe form n(%)	56 (60.2%)
New York Heart Association classification of heart failure	
- class I n(%)	31(33.3%)
- class II n(%)	46 (49.4%)
- class III n(%)	6 (6.4%)
Arterial hypertension	
- stage 1 n(%)	12 (12.9%)
- stage 2 n(%)	46 (49.4%)
- stage 3 n(%)	23 (24.7%)
Smoking n(%)	37 (39.7%)
Alcohol n(%)	31 (33.3%)
Coffee n(%)	59 (63.4%)
Type 2 diabetes n(%)	28 (30.1%)
Dyslipidemia n(%)	67 (72 %)
Snoring n(%)	83 (89.2 %)

The characteristics derived from respiratory polygraphy at baseline and during the three months checkup are shown in Table 2. There was a correlation highly statistically significant between all variables, at baseline and also during the 3 months checkup (p <0.001).

Table 2. Patient characteristics derived from respiratory polygraphy observed at baseline and during three months checkup

Variable	Baseline	3 months	P
Epworth sleepiness scale	11 (7.5;15)	7 (4;10)	<0.001
Apnea hypopnea index	47 (25;70)	12 (7.5;22)	<0.001
Total number of respiratory events	273 (147.5;429)	77 (55;129)	<0.001
Minimum oxygen saturation (%)	76 (68;83.5)	90 (85;95)	<0.001
Average oxygen saturation (%)	88 (84;93)	92 (90.5;94)	<0.001
Longest apnea (sec)	71 (52;98)	35 (25;55)	<0.001
Desaturation index/h	43 (20,5;67.5)	15 (6;22)	<0.001

Epworth Sleepiness Scale significantly decreased by comparing the starting point with the 3-months control after CPAP therapy (p<0.001).

AHI (p=0.005), Epworth Sleepiness Scale (p=0.04) and the total number of respiratory events (p=0.009) decreased more in patients without arterial hypertension compared to those with hypertension. Also AHI decreased more in patients without heart failure then in those with this pathology (p=0.05).

Sleep apnea severity was correlated with obesity (r=0.269; p=0.009). In women, sleep apnea severity (AHI) was correlated with BMI (r=0.592; p=0.005), age (r=0.516; p=0.01), and neck circumference (r=0.584; p=0.005).

There is a linear relationship between AHI and prevalence and severity of hypertension, that is, the more severe the OSA, the higher the risk of hypertension of increasing severity (r=0.206; p=0.04).

No relationship was found between sleep apnea and smoking or alcohol consumption at the 3 months control. AHI did not change differently after treatment, depending on smoking (p=0.6), alcohol (p=0.1). The total number of respiratory events did not depend on smoking (p=0.6) or alcohol (p=0.1). And also, the longest apnea and ODI did not change differently after CPAP, depending on smoking (p=0,8 for longest apnea) (p=0.2 for ODI) or alcohol (p=0.8 for longest apnea) (p=0.4 for ODI).

At one-year control, only 42 (45.1%) of patients continued to use treatment with CPAP, even if is an effective treatment for obstructive sleep apnea (OSA), compliance is a significant problem.

Discussion

All respiratory parameters have improved significantly right after titration. A greater improvement was noted during the 3 months checkup, this confirmed Walia's conclusions according to which CPAP therapy is the mainstay treatment of sleep apnea (Walia et al 2011). Adequate use of CPAP reduces respiratory events and improves clinical symptoms of OSA and daytime sleepiness (Kakkar et al 2007). In our study the Epworth Sleepiness Scale significantly decreased by comparing the starting point with the 3-months control.

There is a predominance of sleep apnea in male (77.4%), obese (30.1% in obesity class 1 and also 30.1% in obesity class 4) and over the age of forty (86 %) (Young et al 1998). Differences in upper airway anatomy, neurochemical mechanisms, the response to arousal, fat distribution and sex hormones all contribute to the pathogenesis of the disease. (Lin C et al 2008)

It is well established that obesity plays an important role in the development of OSA, it is estimated that 60–90% of patients with sleep apnea are obese (Jean Louis et al 2009); 77.4% patients in our study were obese. Obesity is one of the strongest sleep apnea risk factors (Young et al 2005). Fat deposition in the tissues surrounding the upper airway appears to determine a smaller lumen and increased collapsibility of the upper airway, predisposing to sleep apnea (Romero-Corral et al 2010).

In women, sleep apnea severity (AHI) is correlated with BMI, age, and neck circumference. These findings show that, despite marked variation in body weight and fat distribution, the most potent sleep apnea risk factors can predict a small proportion of the variability in sleep apnea severity. (Schwartz et al 2008).

Approximately 40% of patients with sleep apnea suffer from hypertension (Jean Louis et al 2009); 88.1 % patients in our case suffered from hypertension, most of them in stage 2.OSA induced increases in sympathetic activation and contribute to increased blood pressure (Calhoun et al 2010).

The high prevalence of OSA among patients with type 2 diabetes (Foster et al 2009) and vice versa (Lecube et al 2009) has raised the question as how OSA and diabetes interact. OSA is characterized by recurrent upper airway occlusions during sleep which determines specific physiologic disturbances, especially sleep fragmentation and chronic intermittent hypoxia. These disturbances can lead to a cascade of events: activation of the sympathoadrenal system, oxidative stress, systemic inflammation, and changes in adipokines, all increasing the risk of certain diseases: hypertension, metabolic syndrome and type 2 diabetes mellitus (Malik et al 2017). 30.1% of our patients had type 2 diabetes.

Despite the high prevalence of both smoking and sleep apnea, this study does not conclusively establish a clinically significant relationship. OSA therapy, smoking cessation, and abandoning unhealthy lifestyles like: weight gain, alcohol intake, may be effective in improving the quality and duration of life of these patients. (Krishnan et al 2014)

Although many patients with OSA derive subjective benefit from, and adhere to treatment with CPAP, a significant proportion abandon therapy (Wolkove et al 2008), the reason for noncompliance being especially the discomfort caused by the device.

Some of the limitations of the study could be the fact that polysomnography examination was not available.

Conclusion

Sleep apnea patients associated multiple comorbidities. All parameters derived from respiratory polygraphy and also Epworth scale, significantly improved at the 3-months checkup. Sleep

apnea is directly linked to high cardiovascular mortality and morbidity.

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