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Can continuous positive airway pressure improve lower urinary tract symptoms and erectile dysfunction in male patients with severe obstructive sleep apnea syndrome?

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Purpose: We aimed to investigate the effect of continuous positive airway pressure (CPAP) administered for the treatment of obstructive upper airway on lower urinary tract symptoms and erectile dysfunction in male patients.

Materials and Methods: A total of 626 male with suspected obstructive sleep apnea syndrome (OSAS) were evaluated prospectively. Nocturnal polysomnography tests were administered to the male. After application of the exclusion criteria, 54 patients with severe OSAS (Apnea-Hypopnea Index ≥30) were included in the study. International Prostate Symptom Score (IPSS), International Index of Erectile Function (IIEF-15), and nocturia were assessed in all patients before and after CPAP therapy, and prostate volume, total prostate-specific antigen (tPSA), and uroflowmetric measurements were assessed in patients aged >40 years.

Results: The mean age of the 54 patients was 47.06±11.15 years. Post-treatment IIEF scores were better than pre-treatment scores (24.27±7.58 vs. 22.68±8.65, p=0.014). IPSS values, nocturia, and uroflowmetric outcomes significantly improved after CPAP therapy (p<0.05). On the other hand, mean values of body mass index, tPSA, prostate volume, and postvoid residual urine volume did not differ significantly after treatment.

Conclusions: CPAP therapy improves lower urinary tract symptoms, nocturia, and erectile dysfunction in male with severe OSAS.

Keywords: Continuous positive airway pressure; Erectile dysfunction; Lower urinary tract symptoms; Sleep apnea syndromes

INTRODUCTION

Lower urinary tract symptoms (LUTS) impair quality of life and self-esteem and cause significant public health problems. Evidence-based studies have revealed that one in three or four male aged >50 years has moderate to severe LUTS [1,2]. LUTS are divided into three groups: storage symptoms including nocturia, voiding symptoms, and postmicturition symptoms [3]. Nocturia is the most commonly seen entity of LUTS, defined by The International Continence Society as "a complaint that an individual has to wake at night one or more times to void and each void is preceded and followed

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by sleep" [3].

Erectile dysfunction (ED) is defined as the inability to initiate and continue sufficient erection in order to permit satisfactory sexual performance [4]. The overall prevalence of ED in a study conducted by the Turkish Society of Andrology was reported to be 69.2%. It was also noted that the severity and prevalence of ED increases with aging [5].

Sleep is an instinctive and recycling physiological process that is essential for a healthy life. The prevalence of sleep disorders is considered to range from 1% to 5% in male and from 1.2% to 2.5% in female. The prevalence of sleep disorders increases with aging [6]. Obstructive sleep apnea syndrome (OSAS) is one of the leading sleep disorders. In a study conducted in Turkey, the prevalence of OSAS is stated as 0.9% to 1.9% [7]. OSAS is diagnosed with polysomnography testing [8] and is classified by the Apnea-Hypopnea Index [9]. Continuous positive airway pressure (CPAP) administered for the treatment of OSAS is one of the most efficient methods for opening the respiratory system and maintaining a high oxygen saturation in blood.

Nowadays, both OSAS and some urological problems including LUTS and ED are increasing in parallel with increasing elderly populations. Thus, these have become an important public problem. All three disorders are known to be associated with various systemic diseases. Numerous studies have evaluated the presence of both ED and LUTS in patients with OSAS [10,11]. However, studies evaluating whether complaints of LUTS and ED improve after CPAP therapy in patients with OSAS are limited. The purpose of this study was to investigate whether CPAP therapy improves LUTS and ED in patients with severe OSAS.

MATERIALS AND METHODS

This prospective study was conducted in accordance with the Declaration of Helsinki and clinical research ethics principles and was approved by the Bursa Yuksek Ihtisas Training and Research Hospital Ethics Committee (IRB no. 2014/11/01). Written Informed Consent was obtained from all subjects. Male aged ≥18 years and admitted to the neurology department of Bursa Yuksek Ihtisas Training and Research Hospital between December 2017 and October 2019 owing to suspected OSA were included in the current study. Nightlong polysomnography testing was performed by using the Digital PSG system (Alice3; Healthdyne Technologies, Atlanta, GA, USA) in the sleep laboratory of the neurology department [12].

Patients with a history of using alpha blockers or 5-alpha reductase inhibitors, diabetes mellitus, chronic obstructive pulmonary disease, any interventional treatment for transurethral resection of the prostate or benign prostatic hyperplasia, previous urinary system surgery due to urethral strictures or any other reason (urethrotomy, urethroplasty, hypospadias repair, cystolithotomy, etc.); patients diagnosed with prostate cancer or who had undergone a radical prostatectomy operation; those with neurological examination findings or neurologic disease (cerebrovascular event, spinal trauma, multiple sclerosis, etc.); and patients with a history of using diuretics or alcohol consumption were excluded from the study. According to the results of a power analysis (using G*Power 3.1 program) with a 0.80 power value and a 0.05 error, at least 54 patients were needed for statistical analysis.

Patients' demographic data such as age, height, and weight were recorded at the initial stage. All patients were questioned with the International Prostate Symptom Score (IPSS), nocturia, and International Index of Erectile Function (IIEF-15) questionnaires, including the erectile function, orgasmic function, sexual desire, intercourse satisfaction, and overall satisfaction scales. Total prostate-specific antigen (tPSA), prostate volume, and uroflowmetry were measured in patients aged >40 years. Patients were classified according to IPSS scores as having mild (0 to 7), moderate (8 to 19), and severe (20 to 35) symptoms, and according to the IIEF as having severe (0 to 10), moderate (11 to 16), mild-to-moderate (17 to 21), mild (22 to 25), or no ED (26 to 30). These forms were completed by the patients to avoid influence by the practitioner. However, patients were informed about how they could receive information on questions they could not understand. At the second stage, the parameters at the initial stage were applied again at the third month of CPAP therapy.

1. Statistical analyses

Analysis of data was done by using IBM SPSS version 21.0 (IBM Corp., Armonk, NY, USA). Variables were expressed as the means and standard deviations (mean±SD) and numbers (n) and percent (%). Tests of paired t and Wilcoxon signed rank were used for comparison of variables before and after CPAP therapy. Pearson correlation analysis was performed to evaluate the relations between the variables. All p-values <0.05 were considered statistically significant.

RESULTS

A total of 626 patients were evaluated until the required number of 54 patients was reached. After the exclusion of patients with simple snoring, and mild and moderate OSAS,

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Table 1. Baseline characteristics of the study population

Characteristic	n	Mean±SD	Range (min–max)
Age (y)	54	47.06±11.15	22–68
BMI (kg/m^2)	54	30.61±3.83	24.90–43.25
Total AHI	54	50.71±19.12	30–101
Prostate volume (mL) (>40 years old)	37	33.76±12.96	16–66
PSA (ng/mL) (>40 years old)	37	0.97±0.89	0.16–4.70
PVR volume (mL) (>40 years old)	37	26.19±26.93	0–85
VV (mL) (>40 years old)	37	370.29±207.74	150–884

SD, standard deviation; BMI, body mass index; AHI, Apnea-Hypopnea Index; PSA, prostate-specific antigen; PVR, postvoid residual volume; VV, voiding volume.

Table 2. Comparison of values before and after CPAP therapy in male with severe obstructive sleep apnea syndrome

Variable	Pre-treatment	Post-treatment	p-value
Voiding function			
International Prostate Symptom Score	10.38±8.26	7.20±6.65	<0.001
Nocturia	1.92±1.51	1.24±1.21	<0.001
Q_{max} (mL/s)	19.03±10.21	22.40±13.62	0.041
Q_{ave} (mL/s)	8.11±3.27	8.99±3.67	0.012
Sexual function			
IIEF-15 total score	22.68±8.65	24.27±7.58	0.014
Orgasmic function	7.88±3.11	8.33±2.57	0.109
Sexual desire	7.07±2.03	7.42±1.98	0.040
Intercourse satisfaction	9.94±4.20	10.78±3.65	0.020
Overall satisfaction	7.49±2.49	7.80±2.42	0.096

Values are presented as mean±standard deviation.
CPAP, continuous positive airway pressure; Q_{max}, maximum flow rate; Q_{ave}, average flow rate.

91 patients with severe OSAS remained. When we applied the exclusion criteria, 54 male patients were finally enrolled in the study. The mean age of the included 54 patients was 47.06±11.15 years, ranging from 22 to 68 years. No significant difference was found between the groups in terms of body mass index, tPSA, postvoid residual urine volume, and prostate volume. The baseline characteristics of the study population are presented in Table 1.

The mean IPSS score was measured as 10.38±8.26 and 7.20±6.65 before and after CPAP treatment, respectively (Table 2). This difference was statistically significant (p< 0.001). According to IPSS severity, we found a significant increase in the number of patients with mild symptoms and a decrease in the number of patients with severe symptoms (p<0.001; Table 3).

The mean scores for nocturia were 1.92±1.51 and 1.24±1.21 before and after CPAP treatment, respectively. CPAP therapy improved nocturia (p<0.001; Tables 2, 3).

The mean erectile function scores of the IIEF were 22.68±8.65 and 24.27±7.58 before and after CPAP treatment, respectively (p<0.05; Table 2). There was a significant shift from severe to no dysfunction (p=0.014; Table 3). In addition, CPAP treatment improved sexual desire and intercourse satisfaction (p=0.040 and p=0.020, respectively; Table 2).

After CPAP therapy, maximum flow rate (Q_{max}) in patients aged >40 years increased, but the change was not statistically significant. However, there was a significant improvement in average flow rate (Q_{ave}). On the other hand, in a subanalysis including the patients aged >45 years, CPAP treatment significantly improved both Q_{max} and Q_{ave} values (p=0.041 and p=0.012, respectively; Table 2).

According to Pearson's correlation coefficient, difference values between before and after treatment did not correlate with patient age. Namely, CPAP treatment had a similar effect on age groups and gave similar benefits to all patients.

DISCUSSION

There is growing interest in the relationship between OSAS and urological disorders in which ischemia and hypoxia also play a role in the physiopathogenesis. The hypoxia in OSAS develops following apnea and hypopnea. The hypoxia causes oxidative stress, resulting in detrusor instability and spontaneous contractions [13]. Hypoxia also

Table 3. Frequency of nocturia, LUTS, and erectile dysfunction before and after CPAP therapy in male with severe obstructive sleep apnea syndrome (n=54)

Questionnaire scores	Pre-treatment	Post-treatment	p-value
Nocturia (number of nocturia episodes)			<0.001
0	9 (16.7)	18 (33.3)	
1	17 (31.5)	17 (31.5)	
2	11 (20.4)	11 (20.4)	
3	8 (14.8)	4 (7.4)	
4	4 (7.4)	4 (7.4)	
5	5 (9.3)	0 (0.0)	
IPSS severity			<0.001
Mild	24 (44.4)	32 (59.3)	
Moderate	23 (42.6)	19 (35.2)	
Severe	7 (13.0)	3 (5.6)	
ED severity			0.014
No dysfunction	27 (50.0)	30 (55.5)	
Mild	6 (11.1)	12 (22.2)	
Mild to moderate	9 (16.7)	4 (7.4)	
Moderate	6 (11.1)	5 (9.3)	
Severe	6 (11.1)	3 (5.6)	

Values are presented as number (%).
LUTS, lower urinary tract symptoms; CPAP, continuous positive airway pressure; IPSS, International Prostate Symptom Score; ED, erectile dysfunction.

causes endothelial dysfunction in a similar manner [14], and it is believed that LUTS and ED develop as a result. The physiopathologic mechanism by which nocturia develops in patients with OSAS can be explained by the airway obstruction-related hypoxia, hypercapnia, and acidosis, in addition to the intrathoracic negative pressure changes and the episodic increase in sympathetic activity. The secretion of atrial natriuretic peptide increases with the decreased intrathoracic pressure and the hypoxia that develops during sleep. Atrial natriuretic peptide increases glomerular filtration while vasopressin and aldosterone decrease its secretion. The end result is nocturia [15,16]. We therefore believe that OSAS and urologic symptoms could be improved if the ischemia and/or hypoxia were eliminated. We also believe that other disorders accompanying OSAS in which hypoxia plays a role in their physiopathogenesis would also improve.

OSAS is a life-threatening condition characterized by repetitive interruption of breathing due to partial or complete obstruction of the upper respiratory tract during sleep [17]. CPAP, which remains the most effective treatment, was performed for the first time by Sullivan et al. in 1981 [18]. CPAP is a kind of blower system that pumps compressed room air to the patient at the desired pressure [19]. This device is a kind of mechanical ventilator that constantly supplies positive pressured air to the patient's upper respiratory tract through a hose and a mask positioned at the tip of the hose. It has been shown in polysomnography performed in OSAS patients under CPAP treatment that obstructive apnea-hypopnea and snoring disappeared during sleep, increased effort for breathing and heart beats returned to normal, and oxygen saturation remained at a normal level [20].

In the present study, we found a significant improvement in LUTS after 3 months of treatment by CPAP. Similarly, Q_{max} increased in patients older than 40 years, although not significantly so. However, we found a significant improvement in Q_{ave} in those patients. On the other hand, CPAP treatment significantly improved both Q_{max} and Q_{ave} values in patients aged >45 years. This indicates that the improvement became more prominent with increasing age. The ischemia and hypoxia affect bladder function and result in an increase in LUTS [21]. We similarly believe that OSAS creates a synergistic effect with the hypoxia it creates and further increases LUTS. It is possible that LUTS improve and uroflowmetry values with hypoxia are eliminated or decrease. A literature survey has revealed that ours is the only study to demonstrate an improvement in uroflowmetry results with CPAP treatment. We therefore think that our study fills a gap in the literature. The study is the second to investigate the effect of CPAP on both LUTS and ED in patients with severe OSAS. The first study concluded that CPAP treatment eliminates the negative effects of OSAS on ED and LUTS, similar to our findings [22]. Our study will therefore support future meta-analyses as well.

Nocturia is considered when an individual wakes up from sleep to urinate one or more times at night. In a study from Germany with 705 participants, nocturia was suggest-

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ed as the most common cause of sleep interruption [23]. The etiology of nocturia is multifactorial. Pathologic conditions causing nocturia include cardiovascular diseases, diabetes mellitus and insipidus, lower urinary tract obstructions, and sleep disorders [24]. In our study, we found a significant decrease in nocturia after a 3-month CPAP treatment. Studies have found that nocturia is more common among patients with OSAS [25]. In a similar study including 88 patients with OSAS, the amount of nocturia was 3.8 before CPAP treatment, and this value was decreased by 0.7 after 4 months of treatment [26]. Therefore, CPAP treatment was shown to significantly reduce nocturia.

ED may develop as a result of endocrine, vascular, or anatomic disorders, and the incidence and severity of ED is correlated with the severity of OSAS [27]. Hormonal changes, nerve destruction due to hypoxia, vascular changes, and reduced production of nitric oxide related to OSAS have been reported as potential biological mechanisms [27]. It was shown in recent studies that ED is a complication of OSAS [11,28]. Consistent with the literature [22], in our study we found that CPAP treatment improved ED. On the other hand, Perimenis et al. [29] revealed in another study that combination therapy of CPAP and sildenafil was superior to CPAP treatment alone.

The earliest and most common symptom of OSAS is snoring [30]. Almost 35% of patients who present with this symptom have OSAS. Therefore, if patients with snoring are diagnosed with OSAS as a result of polysomnography testing, CPAP treatment in these patients may improve body ischemia and/or oxygen saturation. Thus, we believe that both urological symptoms and other symptoms accompanying OSAS will also be improved.

The prospective design of the study, in which we evaluated the same patients both before and after CPAP treatment, and the minimizing of exposure of the study to external factors increased the importance of this study. On the other hand, the relatively small number of patients may be considered a limitation. Also, we did not evaluate the adherence to CPAP therapy in the subjects. We could not evaluate serum hormones such as atrial natriuretic peptide or serum sex hormones owing to the strict health insurance rules in our country.

CONCLUSIONS

The results of the current study indicate that CPAP therapy provides benefit to patients with severe OSAS in terms of improvement of LUTS, nocturia, and ED. Therefore, patients presenting to the urology clinic with complaints of LUTS and ED should be questioned about OSAS. Moreover, those presenting to a neurology clinic with complaints of OSAS should be asked about LUTS and ED. Better-designed studies with a larger sample size are needed to verify and support our findings.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

AUTHORS' CONTRIBUTIONS

Research conception and design: Soner Coban, Aygul Gunes, and Abdullah Gul. Data acquisition: Soner Coban and Aygul Gunes. Statistical analysis: Abdullah Gul and Soner Coban. Data analysis and interpretation: All of authors. Drafting of the manuscript: Soner Coban, Aygul Gunes, and Abdullah Gul. Critical revision of the manuscript: All of authors. Obtaining funding: None. Administrative, technical, or material support: Soner Coban and Aygul Gunes. Supervision: Soner Coban and Abdullah Gul. Approval of the final manuscript: All of authors.

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