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Continuous positive airway pressure therapy is associated with improvement in overactive bladder symptoms in women with obstructive sleep apnea syndrome

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Introduction To evaluate the impact of continuous positive airway pressure (CPAP) therapy on overactive bladder (OAB) symptoms in women with obstructive sleep apnea syndrome (OSAS).

Material and methods One-hundred and fifty women underwent an overnight polysomnography study between May 2014 and September 2014. Their voiding symptoms were evaluated using the OAB symptom score (OABSS) and International Consultation on Incontinence Questionnaire Short-Form at OSAS diagnosis and approximately 3-months after CPAP therapy. OSAS severity was assessed according to the apnea-hypopnea-index.

Results We evaluated 140 women and 111 of them (79.3%) reported symptoms consistent with OAB. There were no statistically significant differences between OSAS severity with a prevalence of OAB ($p = 0.92$). The prevalence of urinary incontinence (UI) was 35.7% ($n = 50$) and 39.6% ($n = 44$) in all patients and patients with OAB, respectively. There were no statistically significant differences between UI with OAB ($p = 0.58$). Baseline OABSS is comparable between OSAS severity ($p = 0.143$). After 3-months CPAP therapy, OABSS and ICIQ-SF sum scores were significantly decreased in patients with severe and moderate OSAS ($p < 0.01$), however, change of OABSS sum score was insignificant in patients with mild OSAS ($p = 0.44$).

Conclusions CPAP therapy improves the OAB, OABSS and ICIQ-SF scores in women with severe and moderate OSAS. OSAS-induced OAB may be alleviated following CPAP therapy.

Key Words: obstructive sleep apnea syndrome ‹› overactive bladder ‹› continuous positive airway pressure

INTRODUCTION

Obstructive sleep apnea syndrome (OSAS) is a common disorder, which is characterized by instability of the upper airway during sleep, resulting in reduction or elimination of airflow, oxygen desaturation, and sleep disruption [1]. Approximately 4% of middle aged men and 2% of middle aged females are estimated to be affected [1]. OSAS is associated with cardiovascular and cerebrovascular disorders and metabolic dysfunction [2, 3, 4].

The association between OSAS and urologic symptoms such as nocturia, erectile dysfunction, and urgency has been described [5–16]. Sleep disorders may present with nocturia [17]. The mechanism of nocturia in patients with OSAS is related to partial or full obstruction of the airway. An occluded airway leads to a rise in the negative intrathoracic pressures and increased venous blood flow to the heart. Atrial

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natriuretic peptide (ANP) is secreted by the cardiac ventricles and right atrium in response to volume expansion and an increased pressure load [18]. ANP increases sodium and water excretion, inhibits vasopressin release and inhibits the renin-angiotensi n-aldosterone complex. Thus, nocturia derives from nocturnal overproduction of urine in patients with OSAS. Treatment of OSAS with continuous positive airway pressure (CPAP) prevents nocturia arising from OSAS [10].

Overactive bladder (OAB) is another syndrome characterized by urgency, with or without urgency incontinence, frequency and nocturia in the absence of other pathologic features [19]. In Europe, the prevalence of OAB is 4–15% in men and 14–40% in women [20]. The quality of life of sleep and vitality were compromised in 37% of patients with OAB symptoms [21]. There is no previous study, which has investigated the relationship between CPAP therapy and OAB symptoms. In this study, we evaluated the impact of nasal CPAP therapy on OAB symptoms in women with OSAS.

MATERIAL AND METHODS

We prospectively evaluated all female patients with symptoms of OSAS who underwent an overnight polysomnography study between May 2014 and September 2014. We excluded women with diabetes mellitus, neurologic disorders (e.g., diabetes insipidus, multiple sclerosis, disk herniation, stroke, dementia), congestive heart failure, chronic renal failure, physical disabilities, urinary retention, and patients who were taking hypnotics, diuretics or anticholinergics. The study protocol was approved by the local ethics committee. Informed consent was obtained from all participants.

OSAS was diagnosed with an overnight polysomnography study. Heart rate, central and occipital electroencephalogram, electromyography, blood oxygen saturation, extraocular eye movement, respiratory muscle effort, and nasal airflow by thermistor were recorded. Apnea was defined as a complete cessation of airflow lasting more than 10 seconds. Hypopnea was defined as a flow reduction in combination with an oxygen desaturation of more than 4% or an arousal in the electroencephalogram. The apnea hypopnea index (AHI) was the sum of the number of apneas and hypopneas per hour of sleep. OSAS was defined as an AHI of 5 events per hour and the presence of clinical symptoms or AHI of 15 events per hour without any OSAS symptoms [22]. The severity of OSAS was defined by the AHI. A frequency of 5 to 15 events per hour, 15 to 30 events per hour and more than 30 events per hour was considered mild, moderate and severe OSAS, respectively. Minimum oxygen saturation and oxygen desaturation indexes were also determined.

All patients were asked to answer the overactive bladder symptom score (OABSS) and the International Consultation on Incontinence Questionnaire Short-Form (ICIQ-SF) [23, 24]. Validated Turkish translations of these were used [25, 26]. Patients completed self-report questionnaires at two time points: (1) the baseline assessment, after OSAS diagnosis; (2) approximately 3-months after CPAP therapy, patients were contacted by phone.

The OABSS is an 8-item questionnaire for the assessment of OAB including symptoms of daytime frequency, nighttime frequency, urgency and urgency incontinence. The possible range of the score sum is between 0-40 points. OAB was defined as ≥4 points on the OABSS.

The ICIQ-SF is a 4-item questionnaire for the assessment of urinary continence including the frequency of urinary incontinence (UI), perceived amount of urine incontinence and impact on quality of life (QoL). The possible range of the score sum is between 0–21 points. The fourth question asks patients to indicate when urine leaks (never, urge incontinence, stress incontinence, nocturnal incontinence, physically active/exercising incontinence, post-void dribbling, no awareness of urine loss).

Statistical analyses were performed with SPSS version 19.0 for Windows (IBM, NY, USA). Numerical variables were summarized with mean ± standard deviation and categorical variables with frequency and percentage. The significance of differences among groups was assessed by Student's t test or two-way ANOVA, and analysis of categorical variables was examined by the chi-square test. Correlations between independent variables were assessed by Spearman's correlation test. A $p < 0.05$ was considered statistical significance.

RESULTS

One-hundred and fifty patients were screened; 10 patients were excluded, 6 with diabetes mellitus, 2 taking diuretics, 1 with congestive heart failure and 1 with neurologic disorders. The return rate of questionnaires was 100%. The mean age, body mass index, minimum oxygen saturation, oxygen desaturation index, AHI, OABSS and ICIQ-SF parameters for all patients are shown in Table 1. Severe OSAS was determined in 67 of the 140 patients (47.9%), mild and moderate were in 42 (30.0%) and 31 (22.1%) of the 140 patients, respectively. There were no significant differences between OSAS severity with respect to age and BMI.

Overall, 111 of the 140 patients (79.3%) reported symptoms consistent with OAB, which was defined as ≥4 points on the OABSS. There were no statistically significant differences between OSAS severity with a prevalence of OAB (p = 0.92). After 3 months of regular CPAP therapy, the overall prevalence of OAB decreased to 105 of the 140 patients (75.0%), which was statistically insignificant; however the prevalence of OAB in severe and moderate OSAS groups decreased from 78 of the 98 patients (79.6%) to 72 (73.5%), which was statistically significant (p = 0.03) (Table 2).

OABSS and ICIQ-SF sum scores at baseline and after CPAP therapy are shown in Table 2. Baseline OABSS is comparable between OSAS severity (p = 0.143). After 3 months CPAP therapy, OABSS and ICIQ-SF sum scores were significantly decreased in patients with severe and moderate OSAS (p <0.01), however, change of OABSS sum score was insignificant in patients with mild OSAS (p = 0.44). The AHI did not correlate with OABSS sum score (R =-0.062, p = 0.46). The prevalence of UI was 35.7% (n = 50) and 39.6% (n = 44) in all patients and patients with OAB, respectively. There were no statistically significant differences between UI with OAB (p = 0.58). Subgroup analysis of the ICIQ-SF with type of urine leaks revealed no significant differences in OSAS severity. There were no significant differences between UI with CPAP therapy (p = 0.81).

Table 1. *Patient characteristics*

Variables	Mean ± SD (range)
Age (years)	49.3 ±9.6 (22-74)
Body mass index (kg/m2)	29.1 ±4.2 (20-44)
Minimum oxygen saturation (%)	78.0 ±11.1 (40-95)
Oxygen desaturation index	33.0 ±25.0 (116.4-0.9)
AHI	33.5 ±24.7 (5.0-110.3)
OABSS score	9.6 ±7.2 (0-40)
ICIQ-SF score	2.1 ±3.6 (0-14)

AHI – apnea hypopnea index; OABSS – overactive bladder symptom score; ICIQ-SF – International Consultation on Incontinence Questionnaire Short-Form

DISCUSSION

In this study, it was demonstrated that CPAP therapy improves the OAB, OABSS and ICIQ-SF scores in women with severe and moderate OSAS. However, we could not confirm improvement in OAB and OABSS score in mild OSAS. We found that the prevalence of OAB is high among women with OSAS. Our data demonstrates that OSAS severity and AHI did not associate with OAB and OABSS sum score in women. These findings suggest that CPAP therapy for OSAS can provide alleviation of OAB, frequency of UI, perceived amount of urine incontinence and increment of QoL in women with OSAS.

CPAP therapy improves hypoxia, increases plasma NO concentration, and decreases blood pressure and sympathetic over activation [11]. It has been reported that CPAP therapy significantly improves

Table 2. *Comparative data of patients before and after CPAP therapy*

	Baseline	After CPAP therapy	p value
Overall (n=140)			
Prevalence of OAB (No. of patients)	111 (79.3%)	105 (75.0%)	0.31
Mean OABSS score	9.64 ±7.2	7.93 ±6.0	<0.01
Mean ICIQ-SF score	2.10 ±3.6	1.54 ±3.0	<0.01
Mild OSAS (n=42)			
Prevalence of OAB (No. of patients)	33 (78.6%)	33 (78.6%)	1.0
Mean OABSS score	11.02 ±7.6	10.88 ±7.5	0.44
Mean ICIQ-SF score	3.52 ±4.7	3.29 ±4.5	0.04
Moderate OSAS (n=31)			
Prevalence of OAB (No. of patients)	24 (77.4%)	22 (71.0%)	0.5
Mean OABSS score	7.90 ±5.9	6.26 ±4.5	<0.01
Mean ICIQ-SF score	1.90 ±2.9	1.00 ±1.6	<0.01
Severe OSAS (n=67)			
Prevalence of OAB (No. of patients)	54 (80.6%)	50 (74.6%)	0.12
Mean OABSS score	9.58 ±7.5	6.85 ±4.9	<0.01
Mean ICIQ-SF score	1.30 ±2.8	0.70 ±1.5	<0.01
Severe & moderate OSAS (n=98)			
Prevalence of OAB (No. of patients)	78 (79.6%)	72 (73.5%)	0.03
Mean OABSS score	9.05 ±7.0	6.66 ±4.8	<0.01
Mean ICIQ-SF score	1.49 ±2.8	0.80 ±1.5	<0.01

OSAS – obstructive sleep apnea symdrome; OABSS – overactive bladder symptom score; ICIQ-SF – International Consultation on Incontinence Questionnaire Short-Form

the problems of OSAS and that patients with severe OSAS may benefit more from therapy [12]. This observation might explain why CPAP therapy improved OAB in women with severe and moderate OSAS. Patients with OSAS show improved erectile function with CPAP therapy [12, 15]. Another study shows that patients with OSAS and nocturia who are treated with CPAP therapy demonstrate a decrease in the frequency of nocturia episodes [16]. There were no published studies with the relationship between OAB and CPAP therapy in women with OSAS. Epidemiologic surveys of OAB and UI have yielded varying prevalence estimates. In Europe, the prevalence of OAB is 4–15% in men and 14–40% in women [20]. Prevalence of UI is 1.6–24% in men and 4.5–53% in women [27]. The overall prevalence of OAB in patients with OSAS is 39% in men and no data has been published for women before this study [28]. Further, it is shown that the OABSS is significantly higher in men with severe and moderate OSAS, compared in men with mild OSAS [28]. Our study shows that the OABSS is comparable between OSAS severity in women. Another study shows that OSAS is detected in 13 out of 16 women (81%) with OAB, compared with 4 out of 10 healthy women (40%) [29]. OABSS also comprises queries about nighttime frequency; therefore our findings may not be uniquely related to OAB.

The mechanism between OAB symptoms and OSAS is still unclear and may be different in men and women. OSAS is often seen in obese patients, and the risk of OAB is high in these patients [12, 30]. Obesity leads to OAB by way of nerve dysfunction induced by decreased blood flow to the bladder; and OSAS induced hypoxia might increase this mechanism [16, 31]. Another theory based on this phenomenon is that OSAS causes erectile dysfunction by hypoxia-induced occult nerve dysfunction [28]. OAB induced by nerve destruction in diabetes or stroke has been reported [28]. Thus, the mechanism of OSAS induced OAB may be related to hypoxia as well [16, 28]. Another possible mechanism is that malfunction within the central nervous system leads to dysregulation of sleep and micturition [16]. The hypothalamus regulates sleep, arousal and pontine micturition center. The continuous activation of the hypothalamus might induce urgency and might fail in the regulation of sleep and arousal [16].

One of the limitations of this study is that although the analysis was conducted on a sufficient and large population, the study population was not based on a power calculation. Another limitation is that there was no control group or other alternate therapy group such as surgery or mandibular advancement device. The third limitation is the absence of information about daytime and nighttime fluid intake and urine volumes. Finally, it should be noted that further urodynamic studies will be needed to underline our results. To our knowledge, this is the first study with the relationship between OAB and CPAP therapy in women with OSAS.

CONCLUSIONS

This study shows that CPAP therapy improves the OAB, OABSS and ICIQ-SF scores in women with severe and moderate OSAS. These findings have clinical implications, as OSAS-induced OAB may be alleviated following CPAP therapy or women with refractory OAB may be diagnosed with untreated OSAS. We should consider referral of women with refractory OAB to a sleep specialist. Future studies about the relationship of OSAS and OAB should focus on the mechanism of OAB in these patients.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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