Obstructive sleep apnea syndrome and erectile dysfunction: does long term continuous positive airway pressure therapy improve erections?

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Abstract

Objectives: The aim of this age-matched, controlled, prospective clinical study was to investigate frequency and degree of erectile dysfunction (ED) in patients with obstructive sleep apnea syndrome (OSAS) and to evaluate the results of only continuous positive airway pressure (CPAP) therapy on ED in patients with OSAS.

Materials and Methods: A total of 90 patients were evaluated for potential OSAS. They were given an International Index of Erectile Function questionnaire (IIEF) and Beck Depression Inventory. Sixty-two patients with the diagnosis of OSAS were regarded as study group. Twenty-eight patients in whom the OSAS was excluded, were regarded as the control group. Biochemical and hormonal laboratory evaluation were performed. Then all patients underwent a full-night in laboratory polysomnography examination. The degree of OSAS were evaluated by an expert from chest diseases department.

Results: When compared to the control group, a decrease in IIEF-5 scores was found in patients with OSAS. However, this decrease was not statistically significant. After 3 months of CPAP usage in patients with mild to moderate and severe degree OSAS, improvement in IIEF-5 scores was statistically significant. Mean value of IIEF-5 score was 16.63±5.91 before CPAP and were improved up to 20.92±6.79 (P=0.001).

Conclusion: It is not certainly possible to say that OSAS is clearly associated with ED. However, after 3 months of regular CPAP usage, ED complaints in patients with OSAS might improve positively. Trials with larger series may give more conclusive data.

Key Words: Sleep disorder, erectile dysfunction, obstructive sleep apnea syndrome, CPAP

DOI: http://dx.doi.org/10.4314/ahs.v15i1.23

Introduction

Erectile dysfunction (ED) is defined as the inability to initiate and continue sufficient erection in order to permit satisfactory sexual performance[1]. This situation is connected with both physical and psychosocial health and plays an important role in the quality of life of affected men and their partners. In Turkey, the prevalence of ED has been reported as 69.2% in the study that evaluated 1982 men[2].

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Obstructive sleep apnea syndrome (OSAS) should be defined as, the recurrent complete (apnea) or partial (hypopnea) episodes of upper respiratory tract obstruction, and it is often characterized by a decrease in blood oxygen saturation[3]. This is one of the most common sleep disorders. The prevalence was considered as 1-5% for men and 1.2 to 2.5% for women in the adult population. The prevalence increases with age[4]. In a study conducted in Turkey, the prevalence of OSAS was found to be as 0.9- 1.9%[5].

Studies on the patients with OSAS demonstrated that the apneas and hypopneas occuring during the sleep period caused hypoxemia, then hypoxemia caused the activation of the sympathetic nervous system that concomitantly induced cardiovascular system disorders. Consequently, oxidative stress impaired hypothalamic-gonadal axis and lead to psychological depression and decreased libido. In addition, fatigue, decrease in Rapid Eye Movement (REM) sleep period and

neurogenic dysfunction all provoked the deterioration in the quality of erection[6-8]. So, via above etiologic factors, OSAS may lead to ED in men.

Treatment of patients with OSAS may be classified under five headings;[1] lifestyle changes,[2] medical treatment, [3] surgical treatment,[4] oral cavity tools and,[5] continous positive airway pressure (CPAP) therapy. Currently, CPAP therapy was regarded as the gold standard treatment. In a study concerning the results of CPAP treatment performed on ED patients with OSAS, Perimenis et al. compared the results of CPAP therapy with combined therapy (CPAP plus sildenafil therapy). They achieved better results with combined therapy [9]. In our country, in 2008, a study was performed by Taskin et al. including 17 men with severe OSAS[10]. A statistically significant improvement concerning the IIEF scores after one month of CPAP therapy was noticed. They concluded that the CPAP therapy was effective in the treatment of ED. Recently, Shin et al., evaluated the effects of surgical (uvulopalatopharyngoplasty) and non-surgical approaches (CPAP and mandibular advancement devices) on ED and quality of life in 56 cases with OSAS[11]. Patients were evaluated with the Korean version of IIEF-5 after treatment. However, significant increase in IIEF-5 score was only observed in surgically treated group. In 2013, Budweiser et al. assessed the changes in sexual function in men with OSAS after CPAP therapy[12]. CPAP users (n=21) experienced an improvement in overall sexual function (IIEF-15 summary score) when compared to CPAP non-users (n=18). In contrast to the findings of Shin et al., they concluded that CPAP treatment can improve sexual function.

Similarly, in our study, the frequency of ED in OSAS patients was investigated using control groups. We also formed groups from mild-moderate and severe OSAS cases. In addition, we aimed to evaluate the possible effects of CPAP therapy on IIEF scores. For this purpose, we tried to compare the pre-treatment IIEF scores with post-treatment IIEF scores that were held in third month after treatment.

Materials and methods

The study was approved by the Research Ethics Board of our University hospital and all patients signed consent forms to participate in the study. Between the period September 2011- June 2012, 90 patients who applied to the "sleep disorders polyclinic" of chest diseases department of our Faculty with the pre-diagnosis of sleep apnea were involved in the study. All patients were subjected to polysomnography test.

The patients were hospitalized along one night (between the hours of 11:00 pm to 6:00 a.m) in the sleep laboratory equipped with PSG devices -Compumedics, Melbourne, Australia- and -Respironics, Murrysville, PA, USA-, and at least 7 hours of polysomnographic record was obtained. Electroencephalogram, elektrooculogram, electromyogram, and an electrocardiogram results were also recorded. The respiration of patients was monitored by nasal cannula. Chest and abdominal movements, body position, oxygen saturation and snoring sounds were recorded. Polysomnography results were evaluated by an expert (T.Ö.; R.A.) according to the the classification based on 2008 American Academy Sleep Criteria (AASM). Apnea means a respiratory arrest at least 10 seconds or more; but hypopnea expresses a condition in which the respiration continues at least 10 seconds and the flow decreases 50% and saturation drops 3 units, or 30% decrease of flow and a decline of 4 units in saturation.

The sum of the Episodes of apnea and hypopnea was considered as apnea-hypopnea index (AHI). AHI between 5-14 (including 5) plus at least one symptom (snoring, witnessed apnea, excessive daytime sleepiness) was considered as "mild OSAS". AHI score between 15-29 (including 15) was considered as "moderate OSAS", and cases with AHI over 30 were assessed as "severe OSAS". After polysomnography, the patients with an AHI score of less than 5 were regarded as control group.

CPAP usage indications according to AASM 2008 report were considered as; AHI ≥ 15 / hour or AHI ≥ 5 plus the presence of major/obvious symptoms, cardiovascular or cerebrovascular risk factors (hypertension, stroke, excessive daytime sleepiness, ischemic heart disease, insomnia) and existence of mental disorders[13].

CPAP titration was done in an another day for the patients in whom treatment was planned according to the AHI scores. Titration was carried out by an automatic CPAP device (Weinmann, Hamburg, Germany).

In the urology clinic of our hospital, urologists evaluated the ED complaints and possible effects of CPAP treatment. In all cases, a detailed medical and sexual history was taken. The patient's age, presence of erectile dysfunction complaints, the presence of early and late ejaculation, smoking and alcohol consumption, the presence of a systemic diseases, drug use/abuse, physical activity and socio-economic status were questioned and recorded. Detailed physical examination was performed in all patients and the 15-item questionnaire International Index of Erectile Function (IIEF) was completed. IIEF evaluates five domains of sexual function. These are erectile function (6 questions), orgasmic function (2 questions), sexual desire (2 questions), intercourse satisfaction (3 questions), and overall satisfaction (2 questions). Later, a short five-item version of the 15-item IIEF was developed (IIEF-5) to diagnose the presence and severity of ED. IIEF-5 classifies the ED intensity as mild, moderate or severe.

Beck Depression Scale (BDI) was filled in all men who participated in the study. BDI form consists of 21 questions and commonly used to evaluate the psychological status of the patient. After the diagnosis of OSAS, 28 men were subjected to 3-month CPAP therapy. At the end of the therapy, IIEF-15 form was also completed.

The thyroid function, fasting blood glucose, total cholesterol, LDL, HDL, triglycerides, and total testosterone tests were all made in all men. Height and weight of all patients were measured and Body Mass Index (BMI) was calculated for each patient. The calculation was made by the formula of BMI = [weight (kg)/ height (m) ^{2}].

The patients using nitrates, phosphodiesterase type 5 inhibitors and psychotropic medications; patients with hormonal disorders, neuropathic disease, prostate cancer, patients with a history of pelvic trauma, renal transplanted patients, patients with aortic aneurysms, spinal cord injury, penile deformities, alcohol dependence, acute and chronic psychiatric disorders, metabolic and neurological diseases were excluded from the study.

The packaged software of SPSS 13.0 was used in the statistical analysis of this study. The Categorical variables in the data set were given with the frequency and percentage, and constant value measurement variables were given together with the average, standard deviation, median, minimum and maximum values. The Compliance of the continous variables with the normal distribution was controlled by the Shapiro Wilk test. One-way variance analysis was used for the comparison of 3 groups with normally distributed variables. Kruskal-Wallis test was used for the comparison of 3 groups with abnormally distributed variables, and Mann-Whitney U test was used for the comparison of 2 groups. Pearson's Chi-Square test was used for group comparisons of categorical variables. In all analysis, a p value less than 0.05 was considered as statistically significant.

Results

According to the results of polysomnography, 90 patients with OSAS were divided into 3 groups. Men with an AHI score of less than 5 were regarded as control group (n=28; Group 1). Men suffering from mild/moderate OSAS were regarded as Group 2 (n=29), while men with severe OSAS were included in Group 3 (n=33). All men were requested to fill IIEF-5 questionnaire. The CPAP therapy was applied to a total of 28 patients. After 3 months of therapy, they were requested to fill the questionnaire again. Demographic data and clinical parameters for all groups with relevant p values were given in Table 1. Age groups were similar in each groups. No statistically significant difference was noticed when the presence of smoking and alcohol use, diabetes mellitus, hypertension, cardiovascular disease and loss of libido were compared between the groups (p> 0.05, chi-square test). In addition, no difference was observed when groups were compared in terms of daily physical activity and socioeconomic status. When groups were compared in terms of BDI scores, hormonal (thyroid function tests and serum testosterone levels) and biochemical (total cholesterol, LDL, HDL, triglycerides, fasting blood glucose) parameters, no statistically significant difference was observed (p> 0.05; Kruskal-Wallis test) (Table 1).

Table 1. Clinical parameters for all groups with relevant p values

	Group 1 (n=28)	Group 2 (n=29)	Group 3	p value
Age (years)*	46,07 ±12,74	48,97 ±11,3	48,85 ±10,96	0.569**
BMI (kg/m^2)*	28,92±4,32	30,10±4,00	32,14±3,86	0.522**
Hormonal parameters*				p>0.05†
TSH (µIU/ ml)	1,29±0,7 2	1,24±0,6 9	1,36±0,8 0	
free T3 (ng/ dl)	3,69±0,7 8	3,64±0,7 8	3,82±0,9 0	
free T4 (ng/ dl)	1,12±0,18	1,07±0,19	1,02±0,19	
total testosteron (pmol/lt)	327,57±92,16	312,03±69,33	292,58±73,82	
Diabetes Mellitus Present	4	4	5	0.988‡
Absent	24	25	28	
Hypertension Present	9	10	7	0.455‡
Absent	19	19	26	
Cardiovascular disease Present	2	2	1	0.707‡
Absent	26	27	32	
Smoking Present	17	13	18	0.477‡
Absent	11	16	15	
Alcohol consumption Present	11	11	13	1.00‡
Absent	17	18	20	
BDI score*	8,71±7,35	9,17±6,30	12,52±9,89	0.204†
IIEF-5 score*	23,46±5,27	21,82±6,05	19,90±7,05	0.085†

**Values are presented as means ± standard deviations and range*
*** One-way ANOVA*
† Kruskal Wallis test
‡ Chi-square test
IIEF: International Index of Erectile Function
BDI: Beck Depression Scale
TSH: Thyroid stimulating hormone
BMI: Body Mass Index

No correlation was observed between BMI and IIEF-5 scores (p = 0,148, r = 0.154). When the patients were assessed on the basis of IIEF-5 scores, changes in IIEF-5 scores after 3-month CPAP therapy and relevant p values were given in Table 2.

Table 2: Changes in IIEF-5 scores in 28 men who were treated with 3-month CPAP therapy

	Pre-treatment IIEF-5 score	Post-treatment IIEF-5 score	p* value
Group 2 (n=11)	16,45±5, 37 (median:	20,54±5,8 0 (median:	0.005
Group 3 (n=17)	16,76±6,29 (median:19)	21,17±7,53 (median:24)	0.001
Total (n=28)	16,63±5,91 (median:19)	20,92±6,79 (median:23,5)	0.001

** Wilcoxon Signed Rank test*

As seen in Table 3, we observed that the mean minimum (min) and average (ave) oxygen saturation values in each groups were significantly different between each group (p =0.001, Mann-Whitney U test). When the patients were classified into 2 groups according to ave oxygen saturation values ≤89% (n=19; mean IIEF-5 score=17,89±7,89) and above 89% (n=43; mean score=22,09±5,60); statistically significant difference in terms of IIEF-5 scores were noticed (p=0.049; Mann-Whitney U test).

Table 3: Minimum (Min) and Average (Ave) oxygen saturation values according to groups

	Min O_2 saturation	Ave O_2 saturation (%)	p* value
Group 1	89,75±3,02 (median:90)	93,92±1,51 (median:94)	0.001
Group 2	83,17±4,30 (median:83)	92,20±1,89 (median:92)	
Group 3	71,81±12,08 (median:75)	88,90±3,16 (median:89)	
Total	81,05±10,86 (median:84)	91,53±3,15 (median:92)	

** Mann Whitney U test*

The average AHI in groups 1,2 and 3 were 2.72 ± 1.43 (median value: 2.72); 19.84 ± 5.66 (median value: 20.90) and, 58.71 ± 19.48 (median value: 52), respectively. A weak negative correlation between AHI and IIEF-5 scores were documented in correlation analysis (p = 0.013, r = 0.262).

Discussion

Various studies searched the relation between ED and OSAS since 1970's[14-18]. However, very few of these studies examined simultaneously depression which is one of the most important reasons for ED as well. Also, in only a few studies, the change in erectile function after CPAP treatment in OSAS cases were searched. Our main aim in this prospective study was to compare the relation between ED and OSAS in a selective group of patients.

CPAP therapy is regarded as the gold standard treatment by pulmonologists in OSAS treatment[19]. We started 3-month-CPAP therapy in 28 OSAS cases with certain indications (AHI ≥ 15 / hour or AHI ≥ 5 plus the presence of major/obvious symptoms, cardiovas-

cular or cerebrovascular risk factors and existence of mental disorders) . We preferred 3-month therapy, because; after literature review, we concluded that the optimum duration for clinical improvement was defined as 3 months[20,21].

In 2005, Gonçalves et al. examined erectile function in patients with OSAS who received CPAP treatment for a period of one month[22]. They evaluated 98 patients and, found out that ED in patients with OSAS was related with nocturnal hypoxemia. In our study, nocturnal hypoxemia has been searched similarly with oxygen saturation values measured all through the night. When the cut-off value for average oxygen saturation values was taken as 89% for nocturnal hypoxemia; mean IIEF-5 scores of patients with nocturnal hypoxemia were statistically significantly lower than those of patients without nocturnal hypoxemia. We think that, recurrent apnea attacks in patients with OSAS cause hypoxia reperfusion injury and oxidative stress, release of oxygen radicals and endothelial-derived nitric acid and disruptions in its function concomitantly. So, via the effect on NO pathway, nocturnal hypoxemia may cause ED[23].

Depression is the most important psychiatric disorder that may cause ED in patients with OSAS. No statistically significant difference was determined in terms of BDI among patient groups. Similarly, when control and study groups were compared, no statistical significancy was documented. So, we think that inter-group variabilities in terms of BDI scores were minimized. For example, if we had a group with a significantly higher BDI score; IIEF score for that group would probably be affected, and this would be a limiting factor in the evaluation of the relation between ED and OSAS. Because depression is a major risk factor for ED.

One of the most extensive prevalence studies searching the relation between ED and OSAS is the one conducted by Andersen et al[24]. Totally 467 men ranging in age from 20 to 80 have been included in this epidemiological study. When parameters that could effect ED were examined with logistic regression model, they observed that obesity (odds ratio =1.8), low testosterone level (odds ratio= 4.28), disrupted life quality (odds ratio:4.4), AHI over 15 (odds ratio=2.75) and OSAS diagnosis (odds ratio= 2.13) were predictive for ED. In current study, no statistically significant difference was determined between study groups when the average IIEF-5 scores were compared. Although, the p value was insignificant among groups, there were a tendency to lower IIEF-5 scores when the OSAS severity degree increased (Table 1). So, for us, it is not possible to say that OSAS severity is a strong determinant for ED.

For today, age is regarded as the most important determinant in ED etiopathogenesis. Odds ratio for age was 21,65 in the study conducted by Andersen et al[24]. This means that men over 50 have approximately 21 times higher risk for ED than those men in ages between 20-30. Since our study was age matched, in our study, we were able to eliminate the most important determinant in ED etiology.

When the current literature was reviewed, there were also studies which showed no relation between OSAS and ED[18,25,26]. Schiavi et al. investigated nocturnal penile tumescence in 70 men with polysomnographic study that lasted all through the night for four days and found no relation between sleep apnea and ED[26]. In addition, 285 men with ED were examined in a study conducted by Seftal et al. A survey searching OSAS risk factors was made with those patients. According to the results of this study; despite various sleep disorders were determined in patients with ED, no correlation regarding the relation between OSAS and ED was found[27]. However, it should be kept in mind that, OSAS investigation was based on a survey and, no polysomnographic evaluation was made in this study. Later, Margel et al., examined 209 patients similarly through sleep questioning survey and IIEF questionnaire, and all patients were subjected to polysomnographic evaluation[28]. They determined decrease in IIEF scores in patients with OSAS, however this decrease was not statistically significant. They determined statistically significant IIEF decrease only in patients with severe OSAS. In contrast with the findings of Margel et al., in our study, average IIEF-5 scores in men with severe OSAS (group 3) were not significantly different from group 1 and group 2. However, there was a tendency to decrease in IIEF-5 scores when the OSAS severity increased.

Nasal CPAP treatment is effective in patients with OSAS. An interesting study was carried out by Perimenis et al.[29]. In this study, patients with OSAS and ED who received - only CPAP- treatment were compared with -sildenafil plus CPAP- treatment. They found that sildenafil treatment administered together with CPAP is more effective than -only CPAP- treatment. ED degree in patients with severe sleep apnea was also investigated by Taskin et al., and possible benefits of CPAP treatment on ED were searched[10]. Fourty patients with severe OSAS were randomized into 2 treatment groups. While men in the first group were treated with CPAP therapy, men in the second group were treated with antidepressant medication for one month. Mean IIEF-5 score reached 19.06 from 15.71 in the first group, and this increase was statistically significant. We evaluated men with OSAS after "3-month" CPAP treatment. We believed that "1-month" CPAP treatment would not be sufficient for clinical improvement in ED. As seen in Table 2, mean IIEF-5 score, which was 16.45 before CPAP treatment, reached to 20.54 after treatment of patients with mild-moderate OSAS (group 2) (p=0.005). When the patients with severe OSAS were examined, the average IIEF-5 score increased up to 21.17 which was 16.70 before the treatment (p= 0.001). Taskin and colleagues examined patients with severe OSAS only. In addition, we also examined men with mild-moderate OSAS. According to the results of our study, we can say that, men with mild or moderate OSAS may also benefit from 3-month-CPAP treatment as patients with severe OSAS.

In our opinion, if men with OSAS suffer from ED, CPAP treatment should be effective. CPAP therapy combined with oral sildenafil treatment may even be more beneficial as Perimenis et al. previously suggested [29]. On contrary to this opinion, 60 patients with OSAS were treated with CPAP in a study carried out by Margel et al. and long term effects of this treatment were searched. Interestingly, IIEF-5 scores decreased after CPAP treatment[30]. In other words, they concluded that CPAP treatment may disrupt erectile function instead of improving. But, as Taskin et al. already implied in their articles, we think that, CPAP treatment was not administered sufficiently in this study. Margel et al. just administered "one hour CPAP treatment in a week". However, in our study, CPAP therapy was administered "every night for 3 months". We believe that, intensive CPAP treatment is necessary especially in patients with severe OSAS in order to decrease ED complaints.

Both total and free testosterone levels were lower in patients with OSAS according to the results of the study that was carried out by Gambineri et al[31]. In contrast, no statistically significant difference was determined in terms of total testosterone among groups in our study (Table 1). Thus, current study data does not support the hypothesis that OSAS decreases the serum testosterone level.

Several limitations of the present study should be concerned. Although, all polysomnographic measurements and evaluations were made by the same pulmonologists (T.O.;R.A.) who were blinded to the IIEF results and erectile capacity of men in the study groups, the evaluation of erectile dysfunction and depression via IIEF and BDI questionnaires still remain subjective assessment modalities. But, for today, IIEF is regarded as a widely used, multi-dimensional self-report instrument for the evaluation of male sexual function and, is accepted as the "gold-standard" measure for efficacy assessment in clinical trials of ED[32]. Same is true for the BDI questionnaire[33]. Secondly, our sample size is not large enough to make a discrete conclusion. Unfortunately, to the best of our knowledge, no prospective, randomized age-matched clinical trial with larger series has been published evaluating the results of CPAP therapy on ED in patients with OSAS. Further studies focused on this subject may give more conclusive data.

Conclusion

OSAS is not clearly associated with ED. However, after 3 months of regular CPAP usage, ED complaints in patients with OSAS improve positively. Oxygen saturation measurements throughout the night, which was one of the most important tests searching nocturnal hypoxemia, may reveal how much the patient remained hypoxic during the night. In current study, mean IIEF-5 scores were lower in men with nocturnal hypoxemia.

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