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Erectile dysfunction in patient with obstructive sleep apnea: effects of continuous positive airway pressure

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ABSTRACT

Background: Obstructive sleep apnea (OSA) is linked to various health complications, including erectile dysfunction (ED), which is more prevalent in individuals with OSA. This study explored ED in Korean OSA patients and assessed the impact of continuous positive airway pressure (CPAP) therapy on ED.

Methods: A total of 87 male patients with OSA from four different sleep centers underwent physical measurements and completed sleep and mental health (MH) questionnaires, including the Korean version of the International index of erectile function (IIEF), before and three months after initiating CPAP therapy.

Results: After three months of CPAP therapy, the patients demonstrated a significant improvement in ED as measured on the IIEF. However, the study found no significant correlation between the duration of CPAP use and the improvement in IIEF score. It did identify the SF36 quality of life assessment as a significant factor influencing ED improvement after CPAP.

Conclusions: ED is a prevalent issue that escalates with age and is associated with OSA. CPAP therapy has shown potential in alleviating ED symptoms, particularly in those with underlying psychological conditions, although further research is required to confirm these findings and understand the underlying mechanisms.

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Erectile dysfunction; continuous positive airway pressure (CPAP); obstructive sleep apnea (OSA); apnea hypopnea index (AHI); sleep

Introduction

Obstructive sleep apnea (OSA) is a sleep breathing disorder characterized by recurrent obstruction of the upper airway during sleep, resulting in frequent arousals and hypoxemia. It is a relatively common condition observed in 22% of adult males [1]. In the absence of proper medical intervention, this condition may culminate in impaired sleep architecture, characterized by deficient deep sleep and diminished REM sleep. While sleep apnea may not always exhibit symptoms, it is commonly accompanied by pronounced snoring and excessive daytime somnolence. Furthermore, it can increase the risk of several conditions, such as diabetes [2], hypertension [3], cognitive impairment [4], heart disease [5], and stroke [6].

Erectile dysfunction (ED) is a condition characterized by the inability to attain or sustain an erection of adequate strength to facilitate a gratifying sexual experience. This condition is linked to a range of factors, such as structural neurological anomalies, pharmacological agents, psychological elements, and common risk factors. The prevalence of this condition is observed to be around 20% among males aged between 30 and 70 years, and its prevalence tends to rise with advancing age [7]. The prevalence of ED is notably elevated in individuals diagnosed with sleep apnea, with a reported prevalence of up to 69% [8]. Experimental research suggests that the utilization of continuous positive airway pressure (CPAP), which is the conventional treatment for OSA, reduces associated symptoms [9]. The objective of this research is to

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examine the prevalence and attributes of ED among Korean individuals with OSA, as well as to assess changes in ED following CPAP therapy.

Methods

This study enrolled male patients over the age of 18 who were diagnosed with OSA based on a score above 5 on the apnea hypopnea index (AHI) through polysomnography (PSG) in four different sleep centers. All patients had an adaptation period (more than 21 d of use for more than 4 h in 30 consecutive days). The enrollment was conducted prospectively. Exclusion criteria for this study included patients with central sleep apnea, those with anatomical limitations that interfere with CPAP adaptation, and those perceived by the investigator as being unable to sustain participation in this study.

Physical measurements comprised parameters, such as body mass index (BMI), neck/waist circumference, and blood pressure. The study involved administering various sleep questionnaires, such as the Korean version of the Pittsburgh sleep quality index (PSQI), the Epworth sleepiness scale (ESS), the insomnia severity index (ISI), and the Stanford sleepiness scale (SSS). Emotional symptoms were scored using the Beck depression inventory–second edition (BDI-2) and the hospital anxiety depression score (HADS). Quality of life was measured using the short-form health survey version 2 (SF36-v2), and screening for ED was done with the Korean version of the international index of erectile function (IIEF) [10]. A score of 21 or higher on the IIEF indicates the presence of ED.

The PSQI questionnaire comprises 18 items that pertain to various aspects of sleep, such as quality, latency to sleep onset, duration, efficiency, disturbances, use of sleep-related drugs, and daytime dysfunction. The ISI is a comprehensive questionnaire consisting of seven items that assess various aspects of sleep, including awakening, difficulty maintaining sleep, premature awakening, satisfaction with sleep, impact of sleep issues on daily activities, quality of life impairment relative to others, and worry associated with sleep problems. The ISI is a standardized measure of insomnia severity, ranging from 0 to 28. Higher scores on the ISI are indicative of more severe insomnia. To evaluate daytime sleepiness, we utilized both the ESS and the SSS. The ESS is a widely recognized tool that quantifies general levels of daytime sleepiness by asking individuals to rate their likelihood of falling asleep in various situations. The SSS is designed to measure the respondent's current level of

sleepiness. The BDI-II is a standardized assessment tool used to measure depression. It comprises 21 questions and yields a total score of 63, with higher scores indicating greater severity of depressive symptoms. The HADS is a concise questionnaire comprising 14 items, with 7 items each for anxiety and depression. Its primary function is to serve as a screening tool for anxiety and depression disorders, as well as to assess the efficacy of treatment interventions. The cumulative score for the anxiety and depression items is 21 points each, and elevated scores are indicative of increased levels of anxiety and depression.

The SF-36 utilizes a dual-evaluation approach, differentiating between mental health (MH) and physical health (PH) components, thereby offering a holistic assessment of an individual's health status. Specifically, the MH component assesses factors including emotional well-being and social functioning, whereas the PH component concentrates on physical functioning, bodily pain, and role limitations attributable to PH issues.

The CPAP was applied as a therapeutic intervention for individuals diagnosed with OSA who were included in the study. The following evaluation was conducted three months after the initiation of treatment to assess adherence to CPAP, the degree of control of sleep apnea, and the presence of ED. The evaluation of adherence to CPAP therapy was conducted by analyzing the entire day's usage of the device, with a minimum average usage of four hours per day. The data regarding the duration of usage was retrieved by downloading it directly from the CPAP machine. This study was approved by the Institutional Review Board of Keimyung University Hospital (IRB No. DSMC 2021-06-043). All participants provided written informed consent.

The utilization of descriptive statistics is a common practice for summarizing acquired data. This often involves the calculation of frequencies and percentages for categorical data, as well as the determination of mean, standard deviation, minimum, and maximum values for continuous data. The Mann–Whitney test was applied to analyze differences between the ED normal groups in relation to continuous variables, and Fisher's exact test was utilized for categorical variables. The IIEF scores and AHI before and after CPAP treatment were compared using the Wilcoxon test. Linear regression analyses were performed to examine the factors affecting the IIEF score within the group suffering from ED. Additionally, the Mann–Whitney analysis was employed to analyze the differences in various variables between the patient groups categorized by

the presence or absence of ED improvement, as determined by the IIEF. Spearman correlation tests were conducted to determine the presence of a correlation between the factors and the degree of improvement in the IIEF. The statistical analysis was conducted using SPSS version 26.0 software (SPSS Inc., Chicago, IL). The significance level was set at $p < 0.05$.

Results

General characteristics

The study included 129 patients diagnosed with OSA. Of the sample, 42 individuals (32.5%) reported that they did not engage in sexual activity. Participants who reported never being sexually active were excluded from the final analysis. A total of 87 participants reported being sexually active and were included in the final analysis. Of these, 63 reported having ED, and 24 did not report indications of ED. Table 1 shows the characteristics of the ED/normal control group. The ED group was older than the control group ($p = 0.04$). The severity of insomnia as measured on the ISI was higher in the ED group than in the control group, and quality of life as measured on the SF36 was lower in the ED group. The severity of sleep apnea, as measured by the apnea hypopnea Index (AHI) through PSG, was found to be $38.69 \pm 21.45/h$ and $37.07 \pm 20.82/h$ in the respective groups. Within the cohort of patients with OSA, there

Table 1. General characteristics ($n = 87$).

| | Erectile dysfunction ($n = 63$) | Control ($n = 24$) | p Value |
|-----------------------|-----------------------------------|----------------------|--------------------|
| Age | 53.51 ± 12.68 | 46.83 ± 11.00 | 0.040 |
| BMI | 27.36 ± 4.50 | 26.31 ± 3.41 | 0.304 |
| ISI | 11.95 ± 7.02 | 8.17 ± 5.41 | 0.025 |
| SSS | 2.76 ± 1.20 | 2.38 ± 1.24 | 0.091 |
| ESS | 8.51 ± 5.02 | 6.50 ± 3.43 | 0.114 |
| PSQI | 9.18 ± 3.75 | 7.46 ± 3.81 | 0.065 |
| BDI | 12.11 ± 8.94 | 8.50 ± 5.28 | 0.119 |
| BAI | 8.41 ± 8.49 | 4.79 ± 4.09 | 0.100 |
| SF36_M | 68.57 ± 17.91 | 77.33 ± 15.95 | 0.009 |
| SF36_P | 66.95 ± 18.10 | 77.75 ± 13.94 | 0.008 |
| SF36_T | 70.65 ± 18.00 | 80.79 ± 15.58 | 0.012 |
| AHI | 38.69 ± 21.45 | 37.07 ± 20.82 | 0.790 |
| Mild | 11 (17.5) | 3 (12.5) | 0.628 [#] |
| Moderate | 14 (22.2) | 8 (33.3) | – |
| Severe | 38 (60.3) | 13 (54.2) | – |
| Min SaO ₂ | 78.17 ± 7.92 | 80.30 ± 6.74 | 0.370 |
| Mean SaO ₂ | 93.48 ± 4.96 | 94.53 ± 2.26 | 0.329 |
| IIEF score | 14.97 ± 4.81 | 23.21 ± 1.10 | <0.001 |
| Diabetes | 6 (9.5) | 0 | 0.181 [#] |
| Hypertension | 17 (27.0) | 2 (8.3) | 0.082 [#] |

BMI: body mass index; ISI: Insomnia severity index; SSS: Stanford sleepiness scale; ESS: Epworth sleepiness scale; PSQI: Pittsburg's sleep quality index; BDI-2: Beck depression inventory–second edition; SF36-M: short-form health survey-mental health; SF36-P: short-form health survey-physical health; SF36-T: short-form health survey-total; IIEF: International index of erectile function; AHI: apnea hypopnea index; ED: erectile dysfunction/Mann-Whitney.

[#]Fisher's exact test.

was no statistically significant difference observed in the AHI between patients diagnosed with ED and those without ED. Diabetes/hypertension is a well-known risk factor for ED. In this study, we checked for diagnosed diabetes/hypertension and found no difference between the two groups. Of the total participants, 63 (72.4%) patients had ED, and the proportions of ED severity were as follows: 47 (54%) experienced mild ED (IIEF; 12–21), 10 (11.5%) experienced moderate ED (IIEF; 8–11), and 6 (6.9%) experienced severe ED (IIEF; 5–7). There was no difference in the prevalence of ED among the 87 participants, based on the AHI score.

Factors affecting erectile dysfunction in patients with OSA

Potential factors influencing the occurrence of ED were examined, yet no significant variables were found to impact its occurrence.

Erectile dysfunction after CPAP treatment

The study involved 63 individuals who presented with ED. The participants in the ED group presented an average residual AHI of 2.31 ± 1.89 per hour following the application of CPAP therapy ($p < 0.001$). ED, as measured on the IIEF, demonstrated a statistically significant improvement from a mean score of 14.97 ± 4.81 to 16.68 ± 5.46 ($p = 0.001$). A notable improvement in the symptoms of ED was observed, as evidenced by a significant rise in IIEF levels compared to the baseline.

The study examined the relationship between the duration of CPAP therapy and the improvement of ED, with a specific focus on the four-hour threshold. The study's results are presented in Table 2. There were no statistically significant differences in IIEF scores between the two groups, with good and poor adherence separated by the number of hours of CPAP use. The IIEF scores increased from 14.89 ± 4.86 to 16.69 ± 5.47 on average in the good adherence group with 4 h of use, and 11 of the 55 patients who complained of ED after CPAP treatment had normal ED, but this did not reach statistical significance.

Factors that influence the improvement of erectile dysfunction

The study involved administering an ED questionnaire to patients before and after CPAP treatment. Based on the results, the patients were categorized into two

Table 2. Erectile dysfunction improvement by duration of CPAP use ($N = 63$).

| | CPAP use \geq 4 h ($n = 55$) | CPAP use $<$ 4 h ($n = 8$) | p Value |
|-----------------------|----------------------------------|------------------------------|--------------------|
| IIEF (pre-treatment) | 14.89 \pm 4.86 | 15.50 \pm 4.72 | 0.741 |
| Severe ED | 6 (10.9) | 0 | 0.671 [#] |
| Moderate ED | 8 (14.5) | 2 (25.0) | – |
| Mild ED | 41 (74.5) | 6 (75.0) | – |
| IIEF (post-treatment) | 16.69 \pm 5.47 | 16.63 \pm 5.78 | 0.947 |
| Severe ED | 4 (7.3) | 0 | 0.226 [#] |
| Moderate ED | 7 (12.7) | 3 (37.5) | – |
| Mild ED | 33 (60.0) | 3 (37.5) | – |
| Normal | 11 (20.0) | 2 (25.0) | – |

CPAP: continuous positive airway pressure; IIEF: International index of erectile function; ED: Erectile dysfunction/Mann–Whitney.

[#]Fisher's exact test.

Table 3. Influential factors in erectile dysfunction improvements ($n = 63$).

| | Improvement group ($n = 42$) | No-improvement group ($n = 21$) | p Value |
|---|--------------------------------|-----------------------------------|--------------------|
| Age | 52.38 \pm 13.74 | 55.76 \pm 10.18 | 0.275 |
| BMI | 27.63 \pm 4.88 | 26.83 \pm 3.69 | 0.646 |
| Diabetes | 3 (7.1) | 3 (14.3) | 0.391 [#] |
| Hypertension | 7 (33.3) | 10 (23.8) | 0.549 [#] |
| ISI | 11.36 \pm 6.97 | 13.14 \pm 7.14 | 0.336 |
| SSS | 2.74 \pm 1.15 | 2.81 \pm 1.33 | 0.817 |
| ESS | 8.29 \pm 5.14 | 8.95 \pm 4.86 | 0.461 |
| PSQI | 8.76 \pm 3.61 | 10.00 \pm 3.96 | 0.188 |
| BDI | 12.17 \pm 9.53 | 12.00 \pm 7.84 | 0.831 |
| BAI | 8.10 \pm 8.31 | 9.05 \pm 9.02 | 0.671 |
| SF36_MH | 66.60 \pm 17.68 | 72.52 \pm 18.15 | 0.250 |
| SF36_PH | 65.55 \pm 17.04 | 69.76 \pm 20.22 | 0.326 |
| SF36_Tot | 69.21 \pm 17.07 | 73.52 \pm 19.85 | 0.291 |
| Baseline AHI | 36.50 \pm 22.23 | 43.07 \pm 19.56 | 0.175 |
| Residual AHI | 2.09 \pm 1.76 | 2.77 \pm 2.09 | 0.275 |
| CPAP treatment time per day (hour, based on total days) | 4.68 \pm 1.74 | 5.05 \pm 1.61 | 0.449 |
| CPAP treatment time per day (hours, based on using day) | 5.54 \pm 1.38 | 5.82 \pm 1.19 | 0.424 |

BMI: body mass index; ISI: Insomnia severity index; SSS: Stanford sleepiness scale; ESS: Epworth sleepiness scale; PSQI: Pittsburgh's sleep quality index; BDI: Beck depression inventory; BAI: Beck Anxiety inventory; SF36-v2: short-form health survey version 2; IIEF: International index of erectile function; AHI: apnea hypopnea index; ED: Erectile dysfunction/Mann–Whitney.

[#]Fisher's exact test.

Table 4. Major factors contributing to erectile dysfunction ($n = 63$).

| | IIEF post–pre |
|--|----------------|
| Age | –0.049 (0.704) |
| BMI | 0.063 (0.623) |
| ISI | –0.013 (0.921) |
| SSS | 0.051 (0.689) |
| ESS | –0.090 (0.483) |
| PSQI | –0.091 (0.480) |
| BDI | 0.142 (0.268) |
| BAI | 0.096 (0.453) |
| SF36_MH | –0.226 (0.076) |
| SF36_PH | –0.236 (0.063) |
| SF36_Tot | –0.271 (0.032) |
| Baseline AHI | –0.173 (0.175) |
| CPAP treatment time per day (hours, based on total days) | –0.023 (0.859) |
| CPAP treatment time per day (hours, based on using day) | –0.031 (0.809) |

Spearman, BMI: body mass index; ISI: Insomnia severity index; SSS: Stanford sleepiness scale; ESS: Epworth sleepiness scale; PSQI: Pittsburgh's sleep quality index; BDI: Beck depression inventory; BAI: Beck anxiety inventory; SF36-v2: Short-form health survey version 2; AHI: apnea hypopnea index.

groups: those who experienced improvement in their ED after CPAP treatment and those who did not. The factors that influenced the results in each group were then analyzed. Table 3 shows the factors affecting the improvement of ED after CPAP treatment, compared

with the no-improvement group. The main factors affecting ED improvement with CPAP was identified (Table 4). Quality of life, scored on the SF36, was a statistically significant factor influencing the improvement of ED after CPAP.

Discussion

The prevalence of ED ranges from 2% in males under 40 years of age to 86% in males aged 80 and older, according to a previous study [11]. Korean men exhibit a prevalence rate of 13.4% for self-reported ED. The prevalence of ED has been related to an assortment of risk factors, including socioeconomic and MH factors [12]. Several studies have suggested a correlation between OSA and ED. A report by Margel et al. found that men with OSA were more likely to have ED than men without OSA [13]. Similarly, a review by Budweiser et al. concluded that OSA appears to be associated with a higher prevalence of sexual dysfunction, including ED [8]. Additional research on the comorbidity of ED and OSA has revealed that OSA may serve as a plausible risk factor for ED [14].

Despite the absence of properly categorized controlled clinical trials and longitudinal prospective studies, there is an opportunity for forthcoming research to yield significant revelations regarding the interplay between the two conditions and potential therapeutic interventions. Studies indicate that the simultaneous presence of both conditions may lead to a diminished quality of life compared to the experience of each condition alone [15]. In situations where there is a co-occurrence of ED and OSA, it is necessary for clinicians to consider the impact on each individual's quality of life. History taking of accompanying symptoms is important when there is a single condition present, such as ED or OSA. When there is suspicion of OSA in ED patients or ED in patients with OSA, appropriate interventions for each condition can improve the patient's quality of life.

Studies have shown that OSA and ED are more likely to co-occur with age of onset. The link between OSA and ED has been demonstrated in several studies. While the exact mechanisms connecting OSA and ED are not fully understood, several hypotheses have been proposed. One is that intermittent hypoxia caused by OSA may lead to dysfunction in the endothelium, which is crucial for erectile function [16]. Another suggested mechanism is that the poor sleep quality associated with OSA could contribute to ED by leading to hormonal imbalances, such as low testosterone levels [17]. However, in the results of this study, no significant variables were found to be associated with the occurrence of ED. Future research involving a larger number of samples will be necessary.

Perimenis et al. reported that men suffering from OSA observed an amelioration in ED symptoms following a six-month regimen of CPAP therapy [18]. Similarly, a study conducted by Zhang et al. demonstrated that CPAP therapy resulted in improved sexual function in male patients with OSA [19]. The mechanism by which CPAP therapy improves ED can be understood through previous research describing the relationship between OSA and ED. By mitigating intermittent hypoxia, CPAP therapy can potentially improve endothelial function, which could subsequently ameliorate ED symptoms [16]. OSA is often associated with sleep fragmentation and deprivation, which can disrupt normal hormonal balance, including testosterone levels. Testosterone is a critical hormone for sexual function. By improving sleep quality, CPAP therapy could potentially rectify these hormonal imbalances, which could consequently improve ED [17].

OSA could also disrupt nocturnal erectile activity due to frequent arousals caused by apnea. CPAP

therapy can reduce these arousals, thereby improving the quality and frequency of nocturnal erections, which are important for maintaining the functional and structural integrity of penile tissues [20]. OSA is also associated with systemic inflammation, which can contribute to ED. CPAP therapy has been shown to reduce systemic inflammation, which could potentially improve ED [21]. More research is needed to further elucidate these mechanisms and their relative contributions to the potential benefits of CPAP therapy for ED.

Another mechanism of CPAP therapy effectiveness suggested by this study is improvement in psychological status, such as anxiety/depression. Anxiety and depression were prevalent in 79.82% and 79.56% of Chinese patients with ED, respectively. The worsening symptoms of ED have been found to be associated with an upward trend in the prevalence and severity of anxiety and depression [22]. Several investigations have identified psychological issues as making a remarkable contribution to the onset of ED. The results of this investigation suggested that the predominant factor contributing to improved outcomes for ED resulting from CPAP treatment is the presence of pre-existing psychological conditions, such as anxiety and depressive mood, as opposed to the absence of such emotional concerns in patients. Many research investigations have documented improvements in cognitive functioning and decreased negative emotional symptoms subsequent to the adoption of CPAP therapy [23, 24]. The potential correlation between the amelioration of psychiatric symptoms, such as depression and anxiety *via* CPAP therapy and the subsequent improvement of ED, a condition strongly impacted by these symptoms, warrants further investigation. Despite the ambiguity of the theory, the findings of this research strongly suggest that the application of CPAP therapy was advantageous in aiding individuals suffering from OSA and comorbid ED. The study found that anxiety scores by BAI were lower in the improved ED group with CPAP treatment group, similar to previous studies, but did not reach statistical significance. The relationship between anxiety and ED is a complex one, so it is difficult to make simplified conclusions and further research is needed.

Prior research has demonstrated that individuals who show greater adherence to their CPAP treatment exhibit notable improvements in psychological symptoms, including depression and anxiety. In this study, the patients were divided into two groups – high and poor adherence – based on a baseline criterion of utilizing CPAP for a minimum of 4 h per day. The

findings of our analysis suggest that the group with high adherence to CPAP therapy exhibited a degree of improvement in the severity of ED. Although CPAP is not conventionally advocated as a primary treatment for ED, the results from our study imply potential benefits of CPAP in mitigating symptoms associated with both sleep apnea and ED in patients presenting with concurrent OSA and ED. Additionally, our data indicates that considering a minimum therapy duration of approximately 4 h may be beneficial; however, further research is necessary to formulate definitive guidelines.

This study is a multicenter, prospective investigation that may offer valuable insights into the management of ED in patients with OSA. Nonetheless, there are some limitations. First, the study did not assess factors, such as sleep environment, including bed partner and the presence of comorbidities, which may impact CPAP therapy. Considering comorbidities and bedroom environmental factors, including the presence of a bed partner, is essential in implementing CPAP therapy for patients with both ED and OSA. Further research is needed to develop appropriate therapeutic protocols. Second, the evaluation of ED was based on self-reported questionnaire assessments, which limited consideration of ED's pathophysiology. The absence of urologic evaluation, which may be related to ED, is an important weakness of this study. The treatment of ED in patients with OSA should be clarified with additional research involving urologic evaluation. Finally, the clinical symptoms of OSA and ED both persist for lengthy periods of time, and this study only examined short-term effects, so it is difficult to make assumptions about long-term effects. Additional research is necessary to explore the long-term impacts of CPAP therapy, particularly its potential to improve quality of life over time.

Conclusion and future directions

These findings suggest that CPAP therapy could potentially improve ED in men with OSA. It is important to note that while CPAP may help improve ED symptoms in some men with OSA, it is not a guaranteed cure for ED, and other treatments may also be necessary. The improvement in ED was greater in the group with psychiatric problems, such as anxiety and depression prior to treatment, which should be considered by clinicians when designing treatment strategies for these patients.

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