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The Evaluation of Benign Prostate Hyperplasia and Chronic Prostatitis Symptoms with Obstructive Sleep Apnea Syndrome Patients

Obstrüktif Uyku Apne Sendromlu Hastalarda Benign Prostat Hiperplazisi ve Kronik Prostatit Semptomlarının Değerlendirilmesi

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Abstract: Obstructive Sleep Apnea Syndrome (OSAS) is a chronic disorder that increases in prevalence with increasing age. Oxidative stress (OS) and inflammation resulting from OSAS are responsible for the etiopathogenesis of many diseases. OS and inflammation have been found to play a role in the etiopathogenesis of benign prostate hyperplasia (BPH) and chronic prostatitis (CP). The present study aims to compare the prevalence of BPH and CP between patients diagnosed with OSAS and non-OSAS volunteers. Included in the study were 102 patients with OSAS and 110 non-OSAS volunteers, all of whom were assessed with the Berlin Questionnaire, the Epworth Sleepiness Scale, the International Prostate Symptom Score (IPSS) and the Chronic Prostatitis Symptom Index (CPSI). No significant difference was found in the age (p=0.267) and body mass index (BMI) (p=0.995) values of the OSAS patients and non-OSAS volunteers. Berlin Questionnaire (p<0.001) and Epworth Sleepiness Scale (p<0.001) positivity was more common among the OSAS patients than in the control group. The IPSS (p<0.001), CPSI pain score (p<0.001) and CPSI urination symptoms (p=0.002) values were higher in the OSAS patients than in the controls. OSAS patients had more BPH and CP symptoms than the controls. The effective treatment of OSAS is important for the prevention of such chronic diseases as BPH and CP that may develop at later stages of life and that can impair the quality of life of the patient.
Keywords: Obstructive Sleep Apnea Syndrome, Chronic Prostatitis, Benign Prostate Hyperplasia

Özet: Obstrüktif uyku apnesi sendromu (OSAS), yaşla birlikte görülme sıklığı artan kronik bir hastalıktır. OSAS sonucu meydana gelen oksidatif stres (OS) ve inflamasyon, birçok hastalığın etyopatogenezinden sorumlu tutulmaktadır. OS ve inflamasyon, benign prostat hiperplazisi (BPH) ve kronik prostatit (CP) etyopatogenezinde yer almaktadır. Çalışmamız OSAS tanılı hastalarda BPH ve CP görülme sıklığının OSAS olmayanlarla karşılaştırılmasını amaçlamaktadır. Çalışmaya 102 OSAS tanılı hasta ve 110 OSAS olmayan gönüllü dahil edildi. Katılımcılara Berlin Anketi, Epworth Uykululuk Anketi, Interantional Prostate Symtom Score (IPSS) ve Chronic Prostatitis Symptom Index (CPSI) anketi uygulandı. OSAS ve OSAS olmayanlar arasında yaş (p=0.267), vücut kitle indeksi(BMI)(p=0.995) açısından farklılık olmadığı görüldü. OSAS grubunda, kontrol grubuna kıyasla Berlin Anketi (p<0.001) ve Epworth Uykululuk Ölçeği (p<0.001) pozitifliğinin daha fazla olduğu görüldü. OSAS grubunda, kontrol grubuna göre IPSS (p<0.001), CPSI ağrı skoru (p<0.001) ve CPSI işeme semptomları (p=0.002) değerlerinin daha yüksek olduğu görüldü. OSAS'lı hastalarda kontrol grubuna göre BPH ve CP semptomlarının daha fazla olduğu gözlendi. OSAS'ın etkin şekilde tedavi edilmesi ilerleyen dönemlerde hastalarda gelişebilecek BPH ve CP gibi yaşam kalitesini olumsuz etkileyen kronik hastalıkların önlenmesi açısından önem arz etmektedir.
Anahtar Kelimeler: Obstrüktif Uyku Apne Sendromu, Kronik Prostatit, Benign Prostat Hiperplazisi

Ethics Committee Approval: All procedures involving human participants were in accordance with the ethical standards of the institutional Afyonkocatepe University Clinical Ethical Committee (AFSU 2011-KAEK-2_2022/405) and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed Consent: This study did not require informed consent.

Authorship Contributions: A.G. and İ.G.C. designed the study; A.G. and İ.G.C. recruited the participants; A.G. and İ.G.C. participated in the data collection; A.G performed the statistical analysis; A.G. and İ.G.C. interpreted the data; A.G. drafted the first manuscript; and A.G. and İ.G.C. critically reviewed the paper.

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1. Introduction

Obstructive Sleep Apnea Syndrome (OSAS) is a clinical condition that occurs secondary to total (apnea) or partial (hypopnea) obstruction of the upper respiratory tract lasting longer than ten seconds, despite the continuation of thoracoabdominal movement during sleep (1). OSAS affects 5–17% of middle-aged people and 20–60% of those above the age of 65 years (2, 3). OSAS is more common in men than women (4, 5), and a strong correlation exists between Body Mass Index (BMI) and OSAS (6). Comorbidities such as hypertension, diabetes, arrhythmia, myocardial infarction, congestive heart failure, pulmonary hypertension, stroke, dyslipidemia and depression are common in patients with OSAS (7, 8), as are urological comorbidities such as erectile dysfunction, nocturia, benign prostate hyperplasia (BPH) and prostate cancer (9-11). Arterial blood oxygen saturation decreases and blood carbon dioxide pressure increases as a result of inadequate alveolar ventilation during apnea episodes associated with OSAS, and hypoxia subsequently develops (12). The development of hypoxia in OSAS leads to increased production of oxidative stress products (OS) and a decreased level of antioxidative products, which in turn contributes to increased systemic inflammation and the pathogenesis of organ damage (13, 14). OS products have been reported in published studies to increase in the blood of patients with OSAS (15-17). OS has been identified as the main mechanism in aging and in the development of chronic diseases, and the increased manifestation of chronic diseases in patients with OSAS than in those without OSAS may be attributable to OS and inflammation (18). OS and inflammation are also known to play role in the etiopathogenesis of BPH (19). The association between OSAS and BPH has been investigated in recent studies (11, 20, 21). A review of literature revealed only a single publication – a database analysis – evaluating the association between OSAS and chronic prostatitis (CP) (9). OS and inflammation have been demonstrated to play role in CP, although its exact etiology remains unknown (22, 23). OS products occurring as a result of OSAS play role in the etiopathogenesis of CP, and this may be the reason for the simultaneous manifestation of OSAS and CP. The present study evaluates the difference, if any, between the prevalence of BPH and CP in patients with and without OSAS, and is the first study with a case-control design to address this issue.

2. Materials and Methods

a. Study Sample

The study included 102 male patients diagnosed with OSAS by polysomnography and 110 male non-OSAS volunteers as a control group. All the participants were above the age of 18 years. The patients were informed about the study and their written and verbal consent was obtained in advance. Individuals with uncontrolled diabetes mellitus, uncontrolled hypertension, coronary artery disease, congestive heart failure, major central nervous system disease, cognitive disorder, urological disease and psychiatric comorbidities, and those on antidepressant drugs, those who smoked cigarettes and those who used alcohol, were excluded from the study. Patients younger than 18 years of age, those who declined to take part in the study and those whose surveys contained missing data were excluded from the study. The age and BMI values of the patients were recorded, and the Berlin Questionnaire, Epworth Sleepiness Scale, International Prostate Symptom Score (IPSS) and Chronic Prostatitis Symptom Index (CPSI) were applied to all participants. The differences in the survey scores of the patient and control groups, if any, were evaluated.

b. Measurements

The **Berlin Questionnaire** is used for the surveillance of OSAS in society, and comprises 10 questions in three categories. The categories are evaluated separately, and the risk of OSAS is accepted to be high when two or more categories are evaluated as positive (24). Respondents with two or more positive categories are accepted as Berlin Questionnaire positive.

The **Epworth Sleepiness Scale** is used to assess the status of daytime sleep, and comprises eight questions. Respondents are asked about the likelihood of falling asleep on a normal day during which the patient is not over-exhausted in the presence of certain conditions. The questions are answered on a scale of 0–3, and the scoring method is the same for all questions, with a 0 point indicating no chance of falling asleep, 1 indicating a slight chance of falling asleep, 2 indicating a moderate chance of falling asleep and 3 indicating a high chance of falling asleep. A total score of “10” or more indicates excessive daytime sleepiness (25)

in the respondent, who is thus considered Epworth Sleepiness Score positive.

International Prostate Symptom Score (IPSS) is used to evaluate the frequency of lower urinary tract symptoms associated with BPH which contains seven questions assessing (1) incomplete emptying, (2) frequency, (3) hesitancy, (4) urgency, (5) weak stream, (6) straining to initiate urination and (7) nocturia. The answers are scored (0) for the answer "none of them", (1) for "fewer than 1 out of 5", (2) for "fewer than half", (3) for "almost half of them", (4) for "more than half", and (5) for "all of them". The total score is between 0-35, and as the score increases, the severity of the symptoms increases. (26).

The Chronic Prostatitis Symptom Index (CPSI) is used for the diagnosis of CP and chronic pelvic pain syndrome (CPPS) and for the evaluation of response to treatment. It comprises nine questions evaluating pain and discomfort in the anus, testicles, penis and lower abdomen, and investigates problems related to urination and the effects of these problems on quality of life. High scores should be evaluated regarding CP and CPPS. The scores from the responses to the four sub-questions in question one, the two sub-questions in question two, and the responses to questions 3 and 4 are totaled to obtain the CPSI pain score. The sum of the scores from the responses to questions 5 and 6 gives the total CPSI urination symptoms score. The sum of the scores from the responses to questions 7, 8 and 9 gives the CPSI quality of life score (27).

c. Statistical analysis

All statistical analyses were performed using IBM SPSS Statistics (Version 20.0. Armonk, NY: IBM Corp.). The normality of the variables was analyzed using a Kolmogorov-Smirnov (K-S) test. Continuous variables were expressed as mean±SD, and a Student's t-test and a Mann-Whitney U test were used for the between-group comparison of the means. For categorical variables, a Chi-square test was used to test the differences between the groups, and $p < 0.05$ was set as the level of significance.

3. Results

The study included 102 patients with OSAS (48.11%) and 110 (51.89%) non-OSAS volunteers. The mean age in the OSAS and control groups was 49.41±11.40 (25–79) years and 51.24±9.32 (29–70) years, respectively, with no statistical significance between the groups (p=0.267). The mean BMI in the OSAS and control groups was 31.18±5.34 (19.59–43.60) and 30.81±3.90 (21.47-41.16), respectively, with no statistically significant difference between the groups (p=0.995). In the control group, 26 patients (23.6%) had a chronic disease such as hypertension or diabetes, and 18 patients had a chronic disease in the OSAS group (17.6%). No statistically significant difference was found in the presence of comorbidities between the two groups (p=0.312). The Berlin Questionnaire Score was positive in 77 (75.49%) and 29 (26.36%) respondents in the OSAS and control groups, respectively, and negative in 25 (24.51%) and 81 (73.64%) of the respondents in the OSAS and control groups, respectively. A statistically significant difference was found in the Berlin Questionnaire Scores of the OSAS and control groups (p<0.001). The Epworth Sleepiness Scale score was positive in 49 (48.04%) and 27 (24.55%) of the respondents in the OSAS and control groups, respectively, and negative in 53 (51.96%) and 83 (75.45%) of the OSAS and the control groups, respectively. A statistically significant difference was found in the Epworth Sleepiness Scale score between the OSAS and control groups (p<0.001). The median IPSS scores were 8 (0–26) and 5 (0–34) in the OSAS and control groups, respectively, with a statistically significant difference between the groups (p<0.001). The median CPSI pain scores were 4 (0–18) and 0 (0–14) in the OSAS and control groups, respectively, with a statistically significant difference between the groups (p<0.001). The mean CPSI voiding symptom scores were 2 (0–10) and 1 (0–8) in the OSAS and control groups, respectively, with a statistically significant difference (p=0.002). The median CPSI quality of life scores were 4 (0–11) and 3 (0-10) in the OSAS and control groups, respectively, with no statistically significant difference between the groups (p=0.357). A comparison of OSAS and control group data is presented in Table 1.

Table 1. Comparison of data of the OSAS and the control group

		OSAS (n=102)	**Control** (n=110)	**P**
Age (Year)[a]		49.41±11.40 (25–79)	51.24±9.32 (29–70)	.267
BMI [a]		31.18±5.34 (19.59–43.60)	30.81±3.90 (21.47–41.16)	.995
Berlin Questionnaire	Positive[b]	77 (75.49%)	29 (26.36%)	**<.001**
	Negative [b]	25 (24.51%)	81 (73.64%)	
Epworth Sleepiness Scale	Positive[b]	49 (48.04%)	27 (24.55%)	**<.001**
	Negative [b]	53 (51.96%)	83 (75.45%)	
IPSS[c]		8 (0–26)	5 (0–34)	**<.001**
CPSI-Pain Score [c]		4 (0–18)	0 (0–14)	**<.001**
CPSI-Voiding Symptoms [c]		2 (0–10)	1 (0–8)	**.002**
CPSI-Quality of Life		4 (0–11)	3 (0–10)	.357

[a]Mean±standard deviation [b]Number (%) [c]Median (min-max)
BMI: Body Mass Index, IPSS: International Prostate Symptom Score, CPSI: Chronic Prostatitis Symptom Index

Of the 212 respondents in the study, 106 (50%) were identified as Berlin questionnaire positive, while 106 (50%) were negative. An evaluation was made of the association between Berlin Questionnaire positivity and the IPSS and CPSI voiding and pain scores. The mean IPSS was calculated as 7.77±7.07 and 8.78±7.99 in the Berlin Questionnaire Score positive and negative respondents, respectively, with no statistically significant difference (p=0.472). The mean CPSI voiding symptom scores were 3.09±2.40 and 2.19±2.39 in the Berlin Questionnaire Score positive and negative respondents, respectively. The CPSI voiding symptom score was found to be higher in those with a positive Berlin Questionnaire Score than in those with a negative Berlin Questionnaire Score, and the difference was statistically significant (p=0.001). The mean CPSI pain scores were 3.68±4.12 and 3.26±4.02 in Berlin Questionnaire Score positive and negative respondents, respectively. While the CPSI pain score was higher in the respondents with a positive Berlin Questionnaire Score, the difference was not statistically significant (p=0.343). A comparison of Berlin Questionnaire Positive and negative group data is presented in Table 2.

Table 2. Comparison of data of the Berlin Questionnaire positive and negative group

	Berlin Questionnaire Positive (n=106)	**Berlin Questionnaire Negative (n=106)**	**P**
IPSS[a]	7.77±7.07	8.78±7.99	.472
CPSI-Voiding Symptoms [a]	3.09±2.40	2.19±2.39	**.001**
CPSI-Pain Score [a]	3.68±4.12	3.26±4.02	.343

[a]Mean±standart deviation
IPSS: International Prostate Symptom Score
CPSI: Chronic Prostatitis Symptom Index

Epworth Sleepiness Scale was positive in 76 (35.85%) of the 212 respondents included in the study, and negative in 136 (64.15%). The association between the Epworth Sleepiness Scale, and the IPSS and CPSI voiding and pain scores was evaluated. The mean IPSS was 8.14±6.84 and 8.44±7.97 in the respondents with positive and negative Epworth Sleepiness Scale scores, respectively. No statistically significant difference was found in the IPSS scores of those with positive and negative Epworth Sleepiness Scale scores (p=0.692). The mean CPSI voiding symptom score was 2.96±2.42 and 2.45±2.41 in the respondents with positive and negative Epworth Sleepiness Scale scores, respectively. No statistically significant difference was found in the CPSI voiding scores of those with positive and negative Epworth Sleepiness Scale scores (p=0.73). The mean CPSI pain scores were 3.62±4.18 and 3.45±4.05 in the respondents with positive and negative Epworth Sleepiness Scale scores, respectively. No statistically significant difference was noted in the CPSI voiding scores of the respondents with positive and negative Epworth Sleepiness Scale scores (p=0.73). A comparison of Epworth Sleepiness Scale Positive and negative group data is presented in Table 3.

Table 3. Comparison of data of the Epworth Sleepiness Scale positive and negative group

	Epworth Sleepiness Scale Positive (n=76)	Epworth Sleepiness Scale Negative (n=136)	**P**
IPSS[a]	8.14±6.84	8.44±7.97	.692
CPSI-Voiding Symptoms [a]	2.96±2.42	2.45±2.41	.73
CPSI-Pain Score [a]	3.62±4.18	3.45±4.05	.73

[a]*Mean±standart deviation*
IPSS: International Prostate Symptom Score
CPSI: Chronic Prostatitis Symptom Index

4. Discussion

The frequency of BPH and CP symptoms was found to be higher in the respondents with OSAS than non-OSAS group. Positivity was more common in the Berlin Questionnaire and Epworth Sleepiness Scale scores in the respondents with OSAS than non-OSAS group.

The gradually increasing prevalence of obesity, which provides a basis for the onset of OSAS is a significant global health problem (6). The increased BMI in the respondents with OSAS in the present study supports this fact. Polysomnography is considered the optimum approach to the diagnosis of OSAS, while the Berlin Questionnaire and Epworth Sleepiness Scale are recommended for the same purpose (28). All of the patients in the present study had been diagnosed with OSAS based on polysomnography. In parallel to the findings in literature, Berlin Questionnaire and Epworth Sleepiness Scale score positivity were found to be more common in those with OSAS in the present study when compared to the control group. OSAS is a common disease in society that has been associated with many chronic diseases (29, 30). OS and inflammation develop as a result of the hypoxia occurring in OSAS. The greater prevalence of chronic disease in patients with OSAS than in healthy individuals is an expected finding, since they develop due to a similar pathogenesis (31). Recent studies evaluating the association between OSAS and urological diseases have most often focused on the erectile dysfunction, nocturia and overactive bladder disease groups (32, 33). BPH can negatively affect quality of life, although its etiopathogenesis remains unclear. Androgens and aging have been held responsible for the development of BPH, although inflammation is also known to play role in the etiopathogenesis of BPH (34). The association between OSAS and urologic conditions has been addressed in only a limited number of studies with a database design. Huang et al. compared patients with OSAS with a healthy control group in terms of BPH, and found prostate volume to be higher in those with OSAS than in the control group. They reported this to be attributable to the role of OS and inflammation occurring secondary to OSAS in the etiopathogenesis of BPH (11). The IPSS is used to evaluate the diagnosis of BPH and response to treatment, with higher scores indicating more severe symptoms (26). Arslan et al. made a comparison of patients with severe and mild OSAS in terms of BPH, and reported the IPSS scores in patients with severe OSAS to be higher than in those with mild OSAS, though not to a statistically significant degree (35). BPH was noted to be more prevalent in patients with OSAS in two studies carried out to assess the association of BPH and OSAS in society (9, 36). The higher IPSS scores measuring lower urinary system symptoms associated with BPH in patients with OSAS than in the controls in the present study support the association between OSAS and BPH.

CP/CPPS is a heterogeneous disease with pain and voiding symptoms that severely impairs the quality of life of the patient. The etiopathogenesis of CP/CPPS remains unclear, although infectious agents, and immunological, neurological, endocrinological and psychological causes have been held responsible (37). OS and inflammation have been known to play role in the development of CP (38). There is as yet still no definitive or widely accepted pharmacological treatment approach to the treatment of CP, leading to repeat hospital admissions, lost labor and psychological problems (39). When the literature is evaluated, it is seen that there is only one study in the form of database research examining the relationship between OSAS and CP, and this study reports that CP is more common in patients with OSAS. (9). OS and inflammation caused by OSAS play a role in the etiopathogenesis of CP, and this supports the association between the two diseases. The CPSI is used to evaluate the diagnosis and treatment of

CP/CPPS, with high scores indicating CP/CPPS risk (27). The CPSI pain and voiding scores in the OSAS group were higher than non-OSAS volunteers in the present study, indicating a higher risk of CP in patients with OSAS. The main contribution of the present study is its status as the first case-control study reporting a higher risk of CP in patients with OSAS. The efficient treatment of OSAS is known to decrease inflammation and OS (40), which suggests that the efficient treatment of OSAS can prevent chronic diseases with inflammation and OS in etiopathogenesis.

There are some limitations to the present study, including its single-center study design, and the fact that the questionnaire scores were not re-evaluated after the treatment for OSAS. One of the limitations of the study is the lack of polysomnography in the non-OSAS volunteers group. The findings of the present study should be supported by large-scale, multi-center studies.

5. Conclusion

The increased frequency of diseases such as BPH and CP, in which etiopathogenesis includes OS products and inflammation that are secondary to OSAS, compared to non-OSAS volunteers should be an expected condition. The efficient treatment of OSAS would ultimately result in a decrease in the frequency of chronic diseases that can accompany OSAS. The main contribution of the present study is its status as the first case-control study reporting a higher risk of CP in patients with OSAS.

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