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Is overactive bladder a risk factor for erectile dysfunction? A crosssectional study

Aşırı aktif mesane erektil disfonksiyon için bir risk faktörü müdür? Kesitsel çalışma

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¹ Hitit University, Medical Faculty, Department of Urology, Corum, Turkey ORCID ID of the author(s) AB: 0000-0003-0457-512X MMB: 0000-0001-9006-4275	Abstract Aim: Erectile dysfunction (ED) is a sexual dysfunction characterized by the inability to achieve or maintain penile erection during sexual activity. Many risk factors have been identified in ED-related epidemiological studies. In experimental studies, a relationship is thought to exist between Overactive Bladder (OAB) and ED. We investigated the relationship between OAB and ED, its clinical reflections, and the odds ratio of OAB for ED. Methods: We conducted this cross-sectional prospective study between January-July 2020. Sixty patients referred to the urology outpatient clinic with complaints of OAB (Group 1) and 66 patients without urological complaints (Group 2) were included in the study. Patients' erectile functions were evaluated with the IIEF-5 form. OAB was evaluated with the OAB-V8 form. Results: The groups were similar in terms of age, body mass index, comorbidity, and smoking status. IIEF-5 scores were higher in Group 2 [20.52 (3.51)] compared to Group 1 [18.17 (5.46)] (<i>P</i> =0.036). Correlation analysis between IEF-5 and OAB-V8 scores revealed a negative correlation; it was observed that the IIEF-5 score decreased as the OAB-V8 score increased (r=-0.260, <i>P</i> =0.045). The odds ratio of decreasing IIEF-5 score with each 1-unit increase of OAB-V8 score was 0.164 (<i>P</i> =0.04). It was observed that the patients diagnosed with OAB had lower IIEF-5 scores when they had nocturia. Conclusion: OAB is a risk factor for ED. The presence of nocturia symptoms is remarkable for ED in OAB patients. The effect of OAB should not be ignored in the treatment of ED. Keywords: Erectile dysfunction, IIEF-5, OAB, Overactive bladder Öz
Corresponding author/Sorumlu yazar: Aykut Başer Address/Adres: Hitit Üniversitesi, Tıp Fakültesi, Üroloji Anabilim Dalı, Çorum, Türkiye E-mail: aqut85@windowslive.com Hitis Committee Approval: Approval was received from Hitit University noninvasive clinical research ethics committee with the number 2020-206. All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments. Etik Kurul Onayi: Onay Hitit Üniversitesi noninvaziv Klinik Araştırma Etik Kurulundan 2020-206 onay numarası ile alınmıştır. İnsan katılmışıların katıldığı çalışmalardaki tüm prosedürler, 1964 Helsinki Deklarasyonu ve daha sonra yapılan değişiklikler uyarınca gerçekleştirilmiştir.	 Amaç: Erektil disfonksiyon (ED), cinsel aktivite sırasında penis ereksiyonunun sağlanamaması veya sürdürülememesi ile karakterize bir cinsel işlev bozukluğudur. ED ile ilişkili epidemiyolojik çalışmalarda birçok risk faktörü tanımlanmıştır. Deneysel çalışmalarda Aşırı Aktif Mesane (OAB) ile ED arasında bir ilişki olduğu düşünülmektedir. Bu çalışmamızda OAB ve ED arasındaki ilişkiyi, klinik yansımalarını ve ED için OAB'nin risk oranını araştırmayı amaçladık. Yöntemler: Bu kesitsel çalışmayı Ocak 2020 ve Temmuz 2020 arasında gerçekleştirdik. OAB (Grup 1) şikayetleri ile üroloji polikliniğine başvuran 60 hasta ve ürolojik şikayeti olmayan 66 hasta (Grup 2) çalışmaya dahil edildi. Hastaların erektil fonksiyonları IIEF-5 formu ile aşırı aktif mesane sorgulaması OAB-V8 formu ile değerlendirildi. Bulgular: Gruplar yaş, vücut kitle indeksi, komorbidite ve sigara içme durumu açısından benzerdi. IIEF-5 skorları Grup 2'de [20,52 (3,51)] Grup-1'e [18,17 (5,46)] göre daha yüksek bulundu (<i>P</i>=0,036). IEF-5 score ve OAB-V8 score arasında yapılan korelasyon analizinde negatif korelasyon saptandı; OAB-V8 skoru artıkça IIEF-5 skorunun düşüğü gözlendi (r -0,260, <i>P</i>=0,045). OAB-V8 skorunun her 1 birim artışında IIEF-5 puanınında ki azalma risk oranı 0,164 olarak bulunmuştur (<i>P</i>=0,04). OAB tanısı alan hastalarda noktüri varlığında IIEF-5 skorlarının daha düşük olduğu gözlendi. Sonuç: OAB, ED için bir risk faktörüdür. Noktüri semptomlarının varlığı OAB hastalarında ED için dikkat çekicidir. ED tedavisinde OAB'nin etkisi göz ardı edilmemelidir. Anahtar kelimeler: Erektil disfonksiyon, IIEF-5, OAB, Aşırı aktif mesane
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Introduction

Erectile dysfunction (ED) is a sexual dysfunction characterized by the inability to achieve or maintain penile erection during sexual activity [1]. It is a quite common disease among adult males and its incidence increases with age. With the aging US population, it is predicted that more than 35 million American men will experience ED and that 50% of men will be affected by ED until the age of 50 [2]. In epidemiological studies on ED, the main risk factors were divided into 4 categories: 1-Urological and andrological risk factors, 2- Cardiovascular and metabolic risk factors [3]. The relationship between ED and LUTS under the title of urological and andrological risk factors is confirmed by epidemiological studies and potential common biological mechanisms [4].

According to OAB definition of ICS 2002 [5], overactive bladder (OAB) is a syndrome characterized by symptoms of urgency, with or without urgency incontinence, usually with increased daytime frequency and nocturia (increased night-time urination). It includes lower urinary system symptoms (LUTS). The association of OAB, including lower urinary tract symptoms, with Erectile Dysfunction (ED), which is a urological disorder, was also investigated in the literature [6-10]. It was also indicated that ED had a strong relationship with OAB symptoms [9]. OAB affects 11.8-27.2% of men [8,11,12]. The prevalence of overactive bladder also increases with age, as in ED. Both diseases negatively affect health-related quality of life and psychology [13].

Experimental studies demonstrated that mirabegron, which is used in the treatment of OAB, led to the relaxation of the corpus cavernosum by alpha-1 adrenoceptor blockade and that avanafil, which is a type 5 PDH inhibitor, inhibited the activation of detrusor activated by potassium chloride [14,15]. Both experimental studies and the relationship of ED with LUTS suggest that these two urological diseases may be each other's risk factors or comorbid conditions.

In these studies, the relationship between the Overactive Bladder 8-Question Awareness Tool (OAB-V8) scores and The International Erectile Function Index Questionnaire (IIEF-5) scores of OAB patients and the OAB-V8 scores and IIEF-5 scores of control patients randomly selected from the community without OAB, and the clinical reflections of their responses to the IIEF-5 questions were not investigated.

In this study, we conducted an observational study to investigate this relationship and its clinical reflections and calculate the odds ratio of OAB for ED.

Materials and methods

Study design

This study was designed as a cross-sectional study. The present study protocol was reviewed and approved by the Institutional Review Board of Hitit University School of Medicine Ethics Committee (ethics committee approval date-number: 2020-207). Informed consent was obtained from all subjects when they were enrolled. This study was conducted in accordance with STROBE guidelines for reporting observational studies (www.strobestatement.org).

Study population

As a result of the sample size analysis based on other research findings in the literature, the minimum number of participants in each group was determined as 60 with a 95% confidence level and 80% power.

Sixty patients referred to the urology outpatient clinic with complaints of OAB (diagnosed with OAB for the first time and never received anticholinergic treatment) between January 2020 - July 2020, and 66 control patients without urological complaints were included in the study. The patients were informed about the study and written consent forms were received for participation. Patients' age, height, weight, Body Mass Index (BMI), comorbid disease states, and smoking status were examined.

Evaluation of ED

The sexual activity status of the patients with active sexual lives for the last 12 months in the last 4 weeks was evaluated using the 5-question version of the International Erectile Function Index questionnaire (IIEF-5) (16). This questionnaire consists of 4 questions about sexual function and 1 question about sexual satisfaction. Each question is scored between 1-5 points. Patients who stated that they were using PDH-5 inhibitor were not included in the study.

Evaluation of OAB

OAB was evaluated according to the 2002 ICS definition using the OAB-V8 (Overactive Bladder 8-Question Awareness Tool- V8) form consisting of 8 questions developed by Acquadro et al. [17] for symptom scoring in 2006. In this form, each question is scored between 0-5 points. Among the patients with complaints of OAB, those with active urinary tract infections, interstitial cystitis, neurogenic bladder, excessive fluid intake, and patients using diuretics and similar drugs were excluded from the study. In addition, patients were evaluated in terms of benign prostatic hyperplasia. Patients with uroflowmetry maximum flow rate (Qmax) below 15 milliliters/second and patients with obstructive, stenotic, intermittent voiding patterns were not included in the study. Likewise, according to the EAU and AUA guidelines on digital rectal examination and PSA, patients with suspicious findings were excluded.

Statistical analysis

Statistical analyses were performed using the SPSS version 22 software. The distribution of variables was tested by the Shapiro-Wilk test. Descriptive statistics were presented as mean and standard deviation for normally distributed variables, median, minimum, maximum values for ordered ordinal data, and number and percentage for categorical variables. In the evaluation of numerical data between the groups, the parameters with normal distribution were evaluated by student t test, ordinal data were evaluated by Mann-Whitney U test, and categorical data were evaluated by chi-square test. The relationship between the IIEF-5 score and the OAB-V8 score was examined with the Pearson and Spearman's correlation test. The independent effects of the OAB-V8 score on IIEF-5 score were examined with the linear regression model. The model fit was analyzed with the required residual and fit statistics. The cases with a Type-1 error level below 0.5% were statistically evaluated.

Results

A total of 126 patients, including 60 patients diagnosed with OAB (Group 1) and 66 patients in the control group (Group 2), were included in our study. The mean ages of Groups 1 and 2 were 44.30 (12.63) years and 40.15 (13.41) years, respectively. BMI values were 27.95 (5.85) kg/m² and 26.62 (4.68) kg/m² in Groups 1 and 2, respectively. There was no difference between the groups in terms of age and BMI values (P=0.056, P=0.073). IIEF-5 scores were higher in Group 2 [20.52 (3.51)] compared to Group 1 [18.17 (5.46)] (P=0.036). No difference was found between the groups in terms of diabetes, hypertension comorbidity and smoking. The main demographic data of the groups are presented in Table 1.

When the responses to the questions of the IIEF-5 form between the groups were examined, OAB patients were found to have lower scores in question 2 (When you had erections with sexual stimulation, how often were your erections hard enough for penetration?), question 3 (During sexual intercourse, how often were you able to maintain your erection after you had penetrated your partner?) and question 5 (When you attempted sexual intercourse, how often was it satisfactory for you?) compared to control patients (P=0.010, P=0.048, P=0.006, respectively). The scores of IIEF-5 questions among the groups are presented in Table 2 and Figure 1.

Table 1: Demographic characteristics of the patients

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		Group 1 (OAB) n=60	Group 2 (Control) n=66	P-value
		Mean (SD)	Mean (SD)	
Age (year)		44.30 (12.63)	40.15 (13.41)	0.056
BMI (kg/m ²)		27.95 (5.85)	26.62 (4.68)	0.073
IIEF-5 score		18.17 (5.46)	20.52 (3.51)	0.036
Diabetes Mellitus	Yes n (%)	8 (13.3)	8 (12.1)	0.838
	No n (%)	52 (86.7)	58 (87.9)	
Hypertension	Yes n (%)	10 (16.7)	7 (10.6)	0.320
	No n (%)	50 (83.3)	59 (89.4)	
Smoking	Yes n (%)	21 (35)	23 (34.8)	0.986
	No n (%)	39 (65)	43 (65.2)	

BMI: Body Mass Index, IIEF-5: International Index of Erectile Function-5 Score, SD: Standard deviation Table 2: Comparison of the responses of the groups to the IIEF-5 questions

IIEF-5 questions	Group 1 (OAB)	Group 2 (Control)	<i>P</i> -
	n=60	n=66	value
	median	median	
	(min-max)	(min-max)	
1. How do you rate your confidence that	3 (1-5)	5 (2-5)	0.083
you could get and keep an erection?			
2. When you had erections with sexual	4 (1-5)	4.5 (2-5)	0.010
stimulation, how often were your			
erections hard enough for			
penetration?			
3. During sexual intercourse, how often	4 (1-5)	4 (2-5)	0.048
were you able to maintain your			
erection after you had penetrated			
(entered) your partner?			
4. During sexual intercourse, how	4 (1-5)	4 (2-5)	0.051
difficult was it to maintain your			
erection to completion of intercourse?			
5. When you attempted sexual	4 (1-5)	5 (3-5)	0.006
intercourse, how often was it		· · /	
satisfactory for you?			

IIEF-5: International Index of Erectile Function-5 Score, OAB: Overactive Bladder



Almost never/never A few times (much less than half the time) Sometimes (about half the time) Most times (much more than half the time) Almost adways/always Figure 1: Graphical representation of scores given to IIEF-5 questions between groups

In the correlation analysis of OAB-V8 and IIEF-5 scores of OAB patients, IIEF-5 score was determined to decrease (developed erectile dysfunction) as the OAB-V8 score increased (r -0.260, P=0.045). A statistically significant correlation was found between IIEF-5 scores and the questions on Nighttime urination and Waking up at night because you had to urinate (rho -0.283, P=0.028 and rho -0.316, P=0.014, respectively) (Table 3). Linear regression analysis of OAB-V8 and IIEF-5 scores revealed that the odds ratio of decreasing IIEF-5 score for each 1-unit increase of OAB-V8 score was 0.164 (95% CI: 0.325-0.004, P=0.04).

Table 3: Correlation analysis between IIEF-5 score and OAB-V8 questions

OAB-V8 questions	IIEF-5 score	
	Correlation	<i>P</i> -
	coefficient	value
1. Frequent urination during the daytime hours?	0.579	0.550
2. An uncomfortable urge to urinate?	-0.132	0.316
3. A sudden urge to urinate with little or no warning?	-0.098	0.458
4. Accidental loss of tiny amounts of urine?	-0.207	0.113
5. Nighttime urination?	-0.283	0.028
6. Waking up at night because you had to urinate?	-0.316	0.014
7. An uncontrollable urge to urinate?	-0.071	0.590
8. Urinary incontinence associated with a powerful desire to urinate?	-0.158	0.229

OAB-V8: Overactive Bladder Version 8-Question Awareness Tool

Discussion

This is an observational study investigating the relationship between OAB and ED using ICS definitions. In previous studies, it was indicated that sexual activity and satisfaction decreased with LUTS [18-20]. The association of OAB, including lower urinary tract symptoms, with ED was also investigated [6-10]. In the study of Liu et al., it was stated that the groups were affected by the age factor [21]. Aging, diabetes, and hypertension were defined as the risk factors for ED [22]. In our study, fewer elderly population, and the fact that the groups had similar average age minimizes the effect of age on ED and OAB. Furthermore, similar comorbidities also provided isolated examination of ED and OAB.

In their study including 502 OAB patients, Erwin et al. [10] found the risk coefficient of OAB for ED as 1.5. They also found that the odds ratio of OAB was similar to the ED odds ratio of hypertension and diabetes [10]. Amano et al. [23] indicated that OAB was a risk factor of ED and that this odds ratio was 1.12. Liu et al. [7] found that the odds ratio of severe ED for OAB was 2.36 in patients with type 2 diabetes. In another

study, LUTS ED odds ratio was reported as 2.2 [24]. In our study, OAB was determined as a risk factor for ED. This odds ratio was lower than the odds ratios indicated in the literature. However, in our study, the study groups were fewer, they were diagnosed with OAB for the first time and had not received prior treatment for OAB. The similarity between the patients with OAB and the control group patients in terms of risk factors such as hypertension, diabetes, and smoking defined for ED may have led to the lower result of this ratio.

With regards to the relationship between OAB and ED, Erwin et al. [10] showed that urinary symptoms decreased the frequency of sexual activity or prevented participation in sexual activity. In the same study, it was also stated that nocturia and urge incontinence had strong negative effects on ED. Similarly, Liu et al. [7] determined that urge and nocturia had strong effects on ED. In our study, we determined that the patients with OAB had lower IIEF-5 scores compared to the healthy control group. We think that OAB may have a negative effect on Erectile function. Akin to the literature, we determined that nighttime urination and waking up at night because you had to urinate negatively affected IIEF-5 scores. However, we could not find comparable results for urge incontinence. In our study, unlike the literature, we determined that the scores of questions 2, 3 and 5 (erection for penetration, maintaining the erection and satisfaction with sexual intercourse) in the IIEF-5 inquiry form were lower among men with OAB compared to healthy controls. One of the results we obtained in our study was that the responses given to these questions (although there is a need to be supported by studies with a larger number of patients) may be inexpressible OAB symptoms. The effect of OAB should not be ignored in the treatment of ED. OAB should be investigated in those who do not respond to ED treatment. In the literature, sexual functions were reported to improve after anticholinergic treatment in female patients with OAB [25-27]. This was not studied for male patients. There is a need for studies examining the erectile functions of ED patients with OAB after OAB treatment.

Limitations

This study has some limitations, one of which was the small study population. Regarding other reasons, although the study groups were similar in terms of hypertension, diabetes, and smoking, which are known risk factors for ED, patients with these factors were affected by the time they had these risk factors. The effects of nocturia on sleep quality and quality of life may also have effects on erectile function. Furthermore, patients diagnosed with OAB may also be affected by these factors since it was unknown how long the disease existed.

Conclusion

OAB and ED prevalence increase with age. OAB is a risk factor for ED. ED patients with OAB have difficulties in achieving and maintaining erection for penetration and sexual satisfaction. The presence of the symptoms of nocturia is remarkable for ED in OAB patients. The effect of OAB should not be ignored in the treatment of ED, and there is a need for studies examining the erectile functions of ED patients with OAB following OAB treatment.

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