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Investigation of Sexual Dysfunction in Patients with Epilepsy with Regular Follow-up in a Tertiary Neurology Clinic

Üçüncü Basamak Bir Nöroloji Kliniğinde Düzenli Takibi Olan Epilepsi Olgularının Cinsel Fonksiyon Bozukluğunun Araştırılması

Sibel Üstün Özek[1], Zeren Öztürk Altun[2]

[1]University of Health Sciences Turkey, Prof. Dr. Cemil Tascioglu City Hospital, Clinic of Neurology, Istanbul, Turkey

[2]University of Health Sciences Turkey, Prof. Dr. Cemil Tascioglu City Hospital, Clinic of Psychiatry, Istanbul, Turkey

Abstract

Objective: We aimed to assess potential sexual dysfunction (SD) in patients with epilepsy who have no known psychiatric disorders or disabilities.

Materials and Methods: In this study, 48 patients with epilepsy and 69 healthy controls participated. The Arizona sexual experiences scale (ASEX) was used to assess five elements of sexual function in both patients and controls, and the total ASEX score was used to screen for possible SD. Association of SD with demographic and clinical factors were analyzed.

Results: In the patient group, 54% were female and 46% were male. The mean age was 39.3±10.4 years in female patients and 40.0±7.1 years in male patients. In female patients, seizures were classified as focal in 57.7% and generalized in 42.3%, while in male patients, seizures were classified as focal in 45.5% and generalized in 54.5%. The mean duration of the disease was 25.7±11.7 years. Male patients with epilepsy had statistically lower ASEX ejaculation subscale scores compared to controls ($p<0.05$). However, the rates of pathological SD based on the total ASEX scores did not differ statistically between the groups ($p>0.05$). ASEX score was not associated with the duration of the disease and the number of antiepileptic drugs used ($p>0.05$).

Conclusion: There was no difference in potential SD between patients with epilepsy and controls. However, compared to controls, male patients with epilepsy potential ejaculation dysfunction. Early detection of SD using ASEX can have a role in ameliorating the quality of life in patients with epilepsy.

Keywords: Sexual dysfunction, sexual function, epilepsy, gender

Öz

Amaç: Epilepsi hastalarında bilinen bir psikiyatrik problem veya ileri derecede özürlülük olmaksızın olası cinsel işlev bozukluğunun (CİB) sıklığını saptamak amaçlanmıştır.

Gereç ve Yöntem: Çalışmaya epilepsi tanısı almış 48 hasta ve 69 sağlıklı kontrol olmak üzere toplam 117 olgu alındı. Tüm hasta ve kontrollere, olası CİB'yi saptamaya yönelik Arizona cinsel yaşantılar ölçeği (ACYÖ) uygulandı.

Bulgular: Hastaların %54'ü kadın, %46'sı erkekti. Hastaların ortalama yaşı kadınlarda 39,31±10,38 (min: 25, maks: 60), erkeklerde 40,00±7,06 (min: 21, maks: 50) olarak saptandı. Kadınlardaki nöbetlerin %57,7'si fokal, %42,3'ü jeneralize; erkeklerdeki nöbetlerin %45,5'i fokal, %54,5'i jeneralize nöbet tipindeydi. Olguların hastalık başlama yaşı ortalama 25,71±11,70 yıldı. Çalışma grubu olguların ACYÖ "orgazm/ejakülasyon" alt boyutundan aldıkları puanlar, kontrol grubu olgulara göre istatistiksel olarak anlamlı düzeyde düşük saptanmıştır. Olguların ACYÖ toplamından aldıkları puanlara göre patolojik olma oranları, gruplar arasında istatistiksel olarak anlamlı farklılık göstermedi ($p>0,05$). ACYÖ ile hastalık süresi ve kullanılan ilaç sayısı arasında istatistiksel anlamlı ilişki yoktu ($p>0,05$).

Sonuç: Çalışmamıza göre bilinen psikiyatrik bir hastalık öyküsü olmayan epilepsi olgularımızda ACYÖ orgazm/ejakülasyon alt ölçeği puanının düşük olması dışında kontrollere kıyasla toplam skor açısından fark yoktu. ACYÖ ölçeğini kullanarak seksüel disfonksiyonu erken saptamak yaşam kalitesini iyileştirmede rol oynayabilir.

Anahtar Kelimeler: Seksüel disfonksiyon, cinsel işlev, epilepsi, cinsiyet

Address for Correspondence/Yazışma Adresi: Sibel Üstün Özek MD, University of Health Sciences Turkey, Prof. Dr. Cemil Tascioglu City Hospital, Clinic of Neurology, Istanbul, Turkey
Phone: +90 532 596 90 90 E-mail: sibelustun@hotmail.com ORCID: orcid.org/0000-0003-1165-2648
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Introduction

Epilepsy is the second most common neurological disease and is a chronic condition that may require long-term treatment. Although symptoms of this disease may be controlled, epilepsy itself or antiepileptic drugs (AEDs) may disrupt the hypothalamo-pituitary axis and cause ovarian or testicular dysfunctions. Sexual function is an important determinant of quality of life, yet sexual dysfunction (SD) is undetected and underreported in both normal individuals and patients with epilepsy. SD may be classified as psychological or organic in origin, and the two most frequently used definitions of SD are the 1992 10th Revision of the International Statistical Classification of Diseases and Related Health Problems criteria of the World Health Organization and the 1994 Fourth Edition of the Diagnostic and Statistical Manual of Mental Disorders-IV criteria of the American Psychiatric Association (1). The Arizona sexual experiences scale ASEX is one of the tools developed to screen SD in various populations and was found to have acceptable reliability and validity.

Increasing evidence suggests that patients with epilepsy, both male and female, have an increased risk of developing SD (2). Previous research reported that SD occurs in 38-71% of male patients and in 2-60% of female patients with epilepsy (3,4,5,6). Erectile dysfunction, hyposexuality, and organic sexual problems are common complaints in men, while lack of sexual desire, orgasmic dysfunction, dyspareunia, and decreased sexual arousal are the prominent features in women (7,8). These findings suggest that both clinicians and patients should acknowledge that epilepsy has a potentially detrimental effect on sexual functioning.

In this study, we aimed to investigate possible SD in patients with epilepsy who have no known psychiatric disorders or severe disabilities. We found that patients with epilepsy and healthy controls did not differ in risk for possible SD based on ASEX total scores. However, low ASEX Ejaculation subscale scores were seen in male patients with epilepsy. Screening for SD using ASEX can potentially have a role in improving the quality of life in patients with epilepsy.

Materials and Methods

The study was approved by the Ethics Committee of Okmeydani Training and Research Hospital dated December 18, 2018 and numbered 4867077-514.10.

The study was conducted between January 2019 and January 2020 at the epilepsy outpatient clinic of the Prof. Dr. Cemil Tascioglu City Hospital, Neurology Clinic. Patients with a definitive diagnosis of epilepsy for at least 1 year and have been receiving treatment were selected for the study and were classified as having focal or generalized seizures. Other demographic and clinical information collected from patients were age, educational status, duration of marriage, disease duration, onset of disease, seizure control, number of AEDs used, and corresponding doses of each drug. Patients were excluded if they have a previous diagnosis of SD, they did not have a regular partner, they used drugs that might cause SD, and they have a previous diagnosis of any psychiatric disorder. Healthy volunteers were invited to participate for the control group.

The ASEX was administered to all patients and controls to detect possible SD. The ASEX form consists of five subscales corresponding to the elements of sexual function, and the questionnaire has sex-specific versions available (9). The validity and reliability of the Turkish version of the scale was evaluated by Soykan (10). Participants with a total ASEX score of 11 or above were considered to be at high risk for SD and a higher score indicates increased SD. The Beck depression index was also administered to all participants to screen for depression. Those with a depression score of 13 or above were excluded from the study.

Written informed consent was obtained from all patients and controls. Participants filled out the questionnaires with their privacy and confidentiality ensured. A detailed explanation was given about the question items that they did not understand.

Statistical Analysis

The Number Cruncher Statistical System 2007 (Kaysville, Utah, USA) program was used for statistical analysis. Descriptive statistical methods (mean, standard deviation, median, frequency, percentage, minimum, maximum) were used while evaluating the study data. The normality of quantitative data was tested with the Shapiro-Wilk test and graphical examinations. Student's t-test was used for comparisons between two groups of quantitative variables with normal distribution, and Mann-Whitney U test was used for comparisons between two groups of quantitative variables without normal distribution. One-Way analysis of variance and binary evaluations with Bonferroni correction were used for comparisons between groups of more than two quantitative variables with normal distribution. Kruskal-Wallis test and Dunn-Bonferroni test were used for comparisons between groups of more than two quantitative variables that did not show normal distribution. Pearson chi-square test and Fisher-Freeman-Halton exact test were used to compare qualitative data. Statistical significance was set at $p<0.05$.

Results

A total of 117 participants were recruited, 48 of whom were patients with epilepsy and 69 were healthy volunteers. The participants were 52.1% (n=61) female and 47.9% (n=56) male. The ages of the participants in the study ranged from 21 to 60, with a mean age of 39.2±8.6 years.

Of the 48 patients included in the study, 54% were female and 46% were male. The mean age of the patients was 39.3±10.4 (min: 25, max: 60) in women and 40.0±7.1 (min: 21, max: 50) in men. The mean duration of years married in patients was 15.2±13.5 (min: 1, max: 45) for women and 15.5±8 (min: 1, max: 35) for men. Mean age and mean duration of marriage were not significantly different between sexes ($p>0.05$). Patients had different educational attainment: 79.1% (n=38) of the patients were primary school or below graduates, 12.8% (n=6) were high school graduates, and 8.5% (n=4) were university graduates. Smokers comprised 16.7% (n=8) of the patients. The disease onset time of the patients ranged from 5 to 59 years, with a mean of 25.7±11.7 years. It was observed that 72.9% (n=35) of the patients used 1 drug, 20.8% (n=10) used 2 drugs, and 6.3% (n=3) used 3 drugs (Table 1).

In female patients, seizures were classified as focal in 57.7% and as generalized in 42.3%, while in male patients, seizures were classified as focal in 45.5% and as generalized in 54.5%. Our patients with generalized epilepsy had idiopathic generalized epilepsy, juvenile myoclonic epilepsy, or undetected onset epilepsy.

The focal group consisted of patients whose focal focus was detected by EEG, imaging, and clinical examination. Disease duration and seizure types were not different between female and male patients (p>0.05) (Table 2).

When comparing between sexes, men in the control group scored significantly lower in the ASEX Desire subscale compared to women in both the patient group and the control group (p=0.010 and p=0.016, respectively). Moreover, male controls had an ASEX Arousal subscale mean score that was significantly lower than the female controls (p=0.026). There were no statistically significant differences between the sexes in terms of the scores in the ASEX Erection/Lubrication and Satisfaction subscales (p>0.05).

When comparing the patient and control groups, the ASEX ejaculation subscale mean score in male patients was significantly lower than ASEX orgasm/ejaculation subscale scores in female patients, female controls, and male controls (p=0.001, p=0.001, and p=0.002, respectively). There was no statistically significant difference in terms of the scores of the ASEX Desire, arousal, erection/lubrication, satisfaction subscale scores between the groups (p>0.05).

Total ASEX score was found to be significantly lower in male patients compared to female controls. However, there was no statistically significant difference between sexes and the groups in terms of the rates of risk for pathological SD based on the total ASEX score (p>0.05, Table 3 and p>0.05, Table 4, respectively).

ASEX total and subscale scores did not differ between epilepsy types (p>0.05). There was no relationship between the number of epileptic drugs patients used and ASEX desire, arousal, erection/lubrication, and orgasm/ejaculation subscale and total scores (p>0.05), and pathological SD according to the total score (p>0.05).

Discussion

In our study, patients and controls were equally distributed according to sex but sex differences in some of the ASEX scores were observed. No difference was found in the patients compared to the controls in most of the ASEX subscales except in ejaculation subscale scores which were significantly lower in male patients than in controls. The ASEX total score of the men in the patient group was lower than the women in the control group. Interestingly, male controls had lower desire than both female patients and controls, and had lower arousal female controls. A meta-analysis revealed that the prevalence of SD was significantly higher in patients with epilepsy than in the general population regardless of sex. Men and women with epilepsy might be at twice and four times higher risk of SD compared to healthy men and women, respectively (2).

Table 1. Demographic characteristics of participants in the study

Age	Min-max (median)	21-60 (40)
	Mean ± SD	39.2±8.6
Sex	**Women**	61 (52.1)
	Men	56 (47.9)
Education (n=48)	**Elementary school or below**	38 (79.1)
	High school	6 (12.8)
	University	4 (8.5)
Duration of marriage (years)	Min-max (median)	1-45 (10)
	Mean ± SD	13.3±10.1
Disease onset time (years) (n=48)	Min-max (median)	5-59 (24.5)
	Mean ± SD	25.7±11.7
Smoking (n=48)	**No**	40 (83.3)
	Yes	8 (16.7)
Number of drugs (n=48)	**No**	7 (14.6)
	1 drug	29 (60.4)
	2 drugs	9 (18.8)
	3 drugs	3 (6.3)

SD: Standard deviation, Min: Minimum, max: Maximum

Table 2. Evaluation of seizure types by sex

			Sex		
		Total	**Female**	**Male**	**p**
		n (%)	**n (%)**	**n (%)**	
Seizure type	**Generalized**	23 (47.9)	11 (42.3)	12 (54.5)	[a]**0.398**
	Focal	25 (52.1)	15 (57.7)	10 (45.5)	-

[a]Pearson chi-square test

Table 3. Evaluation of Arizona sexual function scale subscales and total scores by sex						
		Study group		Control group		
		Women (n=26)	Men (n=22)	Women (n=35)	Men (n=34)	p
Age	Min-max (median)	25-60 (40)	21-50 (41)	28-58 (37)	23-52 (39.5)	[b]0.958
	Mean ± SD	39.3±10.4	40.0±7.1	39.2±9.0	38.7±8.0	-
Duration pf marriage	Min-max (median)	1-45 (10.5)	1-35 (15)	2-35 (10)	1-32 (9)	[c]0.218
	Mean ± SD	15.2±13.5	15.5±8.5	13.1±9.5	10.8±8.3	-
Desire	Min-max (median)	1-6 (3)	1-4 (3)	1-6 (3)	1-6 (2)	[c]0.004**
	Mean ± SD	3.31±1.64	2.45±0.86	3.09±1.29	2.21±1.25	-
Arousal	Min-max (median)	1-6 (3)	1-4 (3)	1-5 (3)	1-5 (2.5)	[c]0.008**
	Mean ± SD	3.38±1.47	2.55±1.06	3.4±1.17	2.53±1.16	-
Erection lubrication	Min-max (median)	1-5 (3)	1-5 (2)	1-5 (3)	1-5 (3)	[c]0.119
	Mean ± SD	3.35±1.06	2.64±1.29	3.03±1.01	2.74±1.26	-
Orgasm ejaculation	Min-max (median)	1-5 (3)	1-4 (2)	2-6 (3)	1-5 (3)	[c]0.001**
	Mean ± SD	3.19±1.1	1.95±0.84	3.57±0.95	3.09±1.22	-
Satisfaction	Min-max (median)	1-5 (3)	1-4 (2.5)	1-6 (3)	1-5 (3)	[c]0.586
	Mean ± SD	2.42±1.1	2.5±1.1	2.66±1.24	2.82±1.11	-
Arizona total	Min-max (median)	5-26 (15)	5-19 (12)	7-25 (15)	6-24 (12)	[b]0.012*
	Mean ± SD	15.5±5.41	12.09±3.57	15.66±4.56	13.44±4.27	-
	Normal	5 (19.2)	6 (27.3)	4 (11.4)	7 (20.6)	[d]0.488
	Pathological	21 (80.8)	16 (72.7)	31 (88.6)	27 (79.4)	-

[b]One-Way ANOVA, [c]Kruskal-Wallis test, [d]Fisher-Freeman-Halton test, *p<0.05, **p<0.01, SD: Standard deviation

Table 4. Evaluation of Arizona sexual function scale subscales and total scores by groups				
		Study	Control	p
Desire	Min-max (median)	1-6 (3)	1-6 (3)	[c]0.260
	Mean ± SD	2.92±1.4	2.65±1.34	-
Arousal	Min-max (median)	1-6 (3)	1-5 (3)	[c]0.912
	Mean ± SD	3±1.35	2.97±1.24	-
Erection Lubrication	Min-max (median)	1-5 (3)	1-5 (3)	[c]0.654
	Mean ± SD	3.02±1.21	2.88±1.14	--
Orgasm ejaculation	Min-max (median)	1-5 (2)	1-6 (3)	[c]0.001**
	Mean ± SD	2.63±1.16	3.33±1.11	-
Satisfaction	Min-max (median)	1-5 (3)	1-6 (3)	[c]0.269
	Mean ± SD	2.46±1.09	2.74±1.17	-
Arizona total	Min-max (median)	5-26 (14)	6-25 (14)	[f]0.478
	Mean ± SD	13.94±4.92	14.57±4.53	-
	Normal	11 (22.9)	11 (15.9)	[a]0.342
	Pathological	37 (77.1)	58 (84.1)	-

[a]Pearson chi-square test, [c]Mann-Whitney U test, [f]Student's t-test, **p<0.01, SD: Standard deviation

In our study, no difference was found between the focal and generalized epilepsy groups. Several studies have evaluated sexual function separately in focal and generalized epilepsy. Patients with temporal lobe epilepsy (especially on the right side) have a significantly higher incidence of SD than those with extratemporal and primary generalized epilepsy and there is limited evidence to show that sexual function improves in patients who become seizure-free following epilepsy surgery (11). In their study, Torun et al. (12) found more SDs in women. Sexual desire, arousal, and orgasm disorders are seen in both genders. In a study evaluating SD in focal epilepsies, a higher rate of SD was found in temporal lobe epilepsy (12). Epileptiform discharges emanating from the temporal lobe

Table 5. Antiepileptic drugs used by sex		
Antiepileptic drug used	**Female**	**Male**
Carbamazepine	4	4
Levetiracetam	9	4
Valproic acid	0	7
Lamotrigine	4	0
Oxcarbazepine	1	1
Phenytoin	0	1
Carbamazepine and levetiracetam	4	2
Topiramat and levetiracetam	1	0
Lamotrigine and levetiracetam	1	0
Valproc acid and levetiracetam	2	0
Phenytoin and levetiracetam	0	1
Carbamazepine and lacosamide	0	1
Zonisamide and lacosamide	0	1

are transmitted via the amygdala-hypothalamic pathway, which could disrupt the normal release of gonadotropics and the basal level of dopamine secretion. This could result in hypogonadism and hyperprolactinemia and cause SD (13). More broadly, there are studies reporting that the incidence of SD is higher in patients with focal epilepsy than in patients with generalized epilepsy (14). On the other hand, some studies contradict these findings. In a study conducted on patients with generalized epilepsies, it was emphasized that premature ejaculation and erectile dysfunction were higher. They emphasized that poor seizure control and depression increased these problems (15). It was also stated that the type of seizure had no effect on sexual function (16).

The duration of the disease could potentially impact the incidence of SD. In the study of Karan et al. (17), it was observed that the sexual functions of female patients with a longer duration of epilepsy were significantly lower. The effect of seizure frequency on sexual function is still controversial. Some researchers reported that the frequency of seizures was not associated with SD symptoms (18).

In our study, the rate of patients who received polytherapy was 28.26%. When the polytherapy and monotherapy groups were compared, no significant difference was found. It was reported that both epilepsy and AEDs might play a causal role in the SD in patients (19). AEDs can cause hormonal changes and cause SD. Some AEDs (i.e. phenobarbital, carbamazepine, and phenytoin) can induce liver enzymes, leading to direct suppression of gonadal testosterone synthesis and disruption of other peripheral sex steroid hormones (20). It was reported that non-enzyme-inducing AEDs (i.e. lamotrigine and levetiracetam) could significantly improve desire, orgasm, and satisfaction (21). In our patient group, the number of carbamazepine and phenytoin use in men and women was similar. However, levetiracetam and lamotrigine were more used in females. Erdal et al. (22) reported high SD in women in their study in which they evaluated patients receiving valproic acid and carbamazepine treatment. Factors associated with SD included triple or multiple drug treatments, and not using anticonvulsant drugs (23). However, with the new treatment strategies, the use of valproic acid in women decreased and more lamotrigine and levetiracetam were used. The curative effects of these were also mentioned (20).

In our study, the drugs used by the patients were quite heterogeneous. When the drugs were reviewed, statistical comparison could not be made because the numbers were heterogeneous and few in number. However, use of valproic acid was significantly higher males than in females, while there were patients using phenytoin and carbamazepine, as well as patients using new generation zonisamide and lacosamide, which could also cause a decrease in libido (24,25). If SD in the patients could be detected early, the complaints could be controlled with medication changes. In a study conducted by Duncan et al. (26) with 118 male patients with epilepsy, SD, especially loss of libido, impotence and decrease in sexual desire, was found to be higher than the control group.

However, results from different studies are contradictory and unclear regarding the relationship between epilepsy and SD. In a previous study, it was shown that the frequency of SD was only 8% in male patients with epilepsy, 13% in males in the control group and 44% in diabetic male patients. They also reached similar results in females. The group they evaluated consisted of well-controlled patients receiving monotherapy, and it was emphasized that epilepsy did not have a deteriorating effect (27). In line with this finding, de Vincentiis et al. (28) found no difference in terms of SD between adolescent female patients with epilepsy and controls. It was thought that the mean duration of epilepsy, frequency and severity of the seizures, use of AED, sample size, the assessment tool of SD, and variable characteristics of the participants might be partly responsible for the heterogeneity. In our results, the total score was found to be similar to the healthy controls.

Psychiatric and psychosocial comorbidities may also play important roles in the development of SD in epilepsy. It is well known that both anxiety and depression can significantly reduce libido and orgasm, and that psychotropic drugs are considered risk factors for sexual disorders (29). The concurrent use of psychotropic drugs in epilepsy may contribute to the development of SD symptoms (30). These confounding effects made it necessary to exclude patients with known diagnosis or potential symptoms of depression.

Study Limitations

The limitation of our study was the small sample size. Several factors presented as obstacles in recruiting patients. These include high rate of intellectual disability, lack of regular marital relations, patient refusal, and an unconducive environment in the outpatient clinic to allow appropriate counseling and education of patients. Although there was no scale that we used to investigate psychosocial factors, the residence, educational status and occupation of the patients and controls were similar. In a previous study, demographic factors associated with SD in patients with epilepsy were age over 40, low educational status, marriage for more than 15 years, poor economic status, history of infertility and irregular menstrual bleeding, few shifts per month, and night shifts.

Conclusion

SD is a neglected condition in patients who are seen at the outpatient clinic. Issues related to sexuality are not always easily expressed and volunteered by patients, and are not always

considered as part of the examination by the health care providers. The fact that the epilepsy is a chronic disorder and the prevalence of psychiatric and sexual problems are common in these patients, addressing SD and providing support are very important interventions in improving the quality of life in patients.

Ethics

Ethics Committee Approval: The study was approved by the Ethics Committee of Okmeydani Training and Research Hospital dated December 18, 2018 and numbered 4867077-514.10.

Informed Consent: Written informed consent was obtained from all patients and controls.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: S.Ü.Ö., Z.Ö.A., Concept: S.Ü.Ö., Design: S.Ü.Ö., Data Collection or Processing: S.Ü.Ö., Z.Ö.A., Analysis or Interpretation: S.Ü.Ö., Literature Search: S.Ü.Ö., Z.Ö.A., Writing: S.Ü.Ö.

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