

Survey on Smoking, Consuming Alcohol, and Using Illicit Drugs in Patients with Epilepsy

Epilepsi Hastalarında Sigara, Alkol ve Uyuşturucu Madde Kullanımının Araştırılması

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ABSTRACT

Introduction: Addiction can be defined as the continuous consumption of addictive substances or repetition of certain behaviors despite adverse consequences. Epilepsy is associated with an increased risk of psychiatric disorders. However, to the best of our knowledge, there is no published data regarding addictions in patients with epilepsy. Considering the high incidence of psychopathology, we planned a survey using a self-report questionnaire to study some of the addictive behaviors in patients with epilepsy and in control subjects.

Methods: Patients from our outpatient epilepsy clinic (n=106) and control subjects (n=96) aged between 18 and 65 years took the 20-question questionnaire that screened for smoking, consuming alcohol, or using other illicit drugs.

Results: Fifty-three percent of patients with epilepsy were male (n=57) and in the control group, 52% were male (n=50) (p=.062). The mean age was 32.66±2.23 years for patients with epilepsy and 35.70±0.59 years for the control group (p=.810). Mean duration of epilepsy was found to be

14.33±11.26 (1–46) years. Majority of patients with epilepsy (84%) had focal epilepsy. Alcohol intake was found to be significantly lower in patients with epilepsy (p=.0001). There was no difference regarding smoking (p=.530) or using illicit drugs between the groups (p=.262). Smoking cigarettes was lower in new onset epilepsies (<5 years) compared with epilepsies of longer duration (p=.031).

Conclusion: Recent studies connote to some common substrates in the pathophysiology of epilepsy and addiction. Therefore, we wanted to evaluate some addictive behaviors in patients with epilepsy. Although this study did not show significant differences other than low frequency of alcohol use in patients with epilepsy and low rate of smoking in patients with epilepsy duration of <5 year, further studies among homogeneous epilepsy subgroups with larger scale along with their neuropsychological profiles may still be required.

Keywords: Epilepsy, smoking, alcohol, illicit drug, addiction

ÖZET

Amaç: Bağımlılık, kişinin aleyhine sonuçlara yol açmasına rağmen bağımlılık yapıcı maddenin sürekli kullanımı ya da belirli bir davranışın tekrarlanması şeklinde tanımlanabilir. Epilepsi hastalarında psikiyatrik hastalıkların görülme riski artmıştır. Fakat bildiğimiz kadarıyla literatürde epilepsi hastalarında bağımlılık konusunu ele alan veriler yer almamaktadır. Epilepsi hastalarında psikopatolojilere sıkça rastlanılması nedeniyle bu çalışmada epilepsi hastaları ve kontrol grubunda bazı bağımlılık yapıcı maddelerin kullanımını araştıran bir anket uygulandı.

Yöntem: Çalışmamıza 18-65 yaşları arasında kliniğimiz epilepsi polikliniğinde takipli 106 epilepsi hastası dahil edildi. Kontrol grubu 96 kişiden oluşmaktaydı. Katılımcılara sigara, alkol, uyuşturucu madde kullanımını sorgulayan 20 soruluk bir anket uygulandı.

Bulgular: Epilepsi hastalarının %53'ü (n= 57), kontrol grubunun %52'si (n=50) erkeklerden oluşmaktaydı (p=0,062). Ortalama yaş düzeyi epilepsi hastalarında 32,66±12,23, kontrol grubunda 35,70±10,59 olarak hesaplandı (p=0,810). Epilepsi hastalarında ortalama hastalık süresi 14,33±11,26 yıl (1-46) bulundu. Epilepsi hastalarının çoğunluğu (%84)

fokal epilepsi nedeniyle takip edilmekteydi. Epilepsi hastalarında alkol kullanımının belirgin bir şekilde daha az olduğu izlendi (p=0,0001). Her iki grup arasında sigara kullanımı (p=0,530) ya da uyuşturucu madde kullanımı (p=0,262) açısından anlamlı farklılık saptanmadı. Yeni başlangıçlı epilepsi hastalarında (5 yıldan az) sigara kullanımı daha uzun süreli epilepsi hastalarına göre daha düşük oranda gözlemlendi (p=0,031).

Sonuç: Son zamanda yapılan çalışmalar epilepsi ve bağımlılık patofizyolojisinde bazı ortak nörokimyasal faktörleri ve ağları işaret etmektedir. Bu nedenle bu çalışmada epilepsi hastalarında bazı bağımlılık gruplarının değerlendirilmesini amaçladık. Bu çalışmada her ne kadar sağlıklı kontroller ile epilepsi hastaları arasında alkol kullanımı ve 5 yıldan kısa süreli epilepsi hastalarında daha düşük sigara kullanımı dışında anlamlı farklılıklar saptanmasa da, ileride daha geniş katılımcıların ve homojen epilepsi gruplarının dahil edildiği, nöropsikolojik değerlendirmelerin de yer alacağı çalışmalarda epilepsi ve bağımlılık arasındaki olası ilişkilerin ortaya konabileceğini düşünmekteyiz.

Anahtar kelimeler: Epilepsi, sigara, alkol, uyuşturucu madde, bağımlılık

INTRODUCTION

Chronic consumption of illicit drugs and/or alcohol and/or performing persistent behaviors, such as gambling, may be the most disastrous aspects in the addiction spectrum. Addiction can be defined as the continuous consumption addictive substances or repetitive acting of certain behaviors despite adverse consequences (1). It is accepted as a primary, chronic disorder involving brain reward, mo-



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tivation, memory, and related circuitry, resulting in its characteristic biological, psychological, social, and spiritual manifestations, such as tolerance, withdrawal, craving, and dysfunction of interpersonal, social, and occupational relationships (2,3).

The studies regarding the underlying biological mechanisms for substance or behavioral addiction suggest similar pathways for both situations. It has been demonstrated that dopamine release in the nucleus accumbens is required for initial reward feeling and for the initiation of addiction. The repeated exposure to the substance or behavior causes gradual recruitment of the prefrontal cortex and its glutamatergic efferents to the nucleus accumbens that is followed by cellular adaptations occurring in a chronological fashion. Hence, the process takes place in the mesolimbic pathway and extends to the amygdala (3,4).

It is generally accepted that epilepsy is associated with an increased risk of psychiatric disorders such as depression, anxiety, psychosis, and suicide in the pre- and post-diagnostic period. These associations connote common underlying pathophysiological mechanisms that both lower seizure threshold and increase the risk for psychiatric disorders and suicide (5). Another suggestive statement implying the underlying common mechanisms between epilepsy and psychopathologies comes from the fact that an increased risk of psychopathology in epilepsy outweighs the same risk in other chronic medical or neurologic conditions (6).

Advances in the neuroscience would hold potential for elucidation of pathways between seizures, other neurologic diseases, psychopathology, and addiction. Recently, it has been proposed that epilepsy is a network disorder that occurs because of disturbance or interruption in the harmony of cortical and subcortical pathways. Some studies suggest that the involvement of dopamine-modulated basal ganglia circuits influencing thalamocortical projections may be a feature of both generalized and focal epilepsies (7).

To the best of our knowledge, there is no published data regarding addictions in patients with epilepsy. Considering the high incidence of psychopathology and recent developments regarding the underlying common mechanisms of psychiatric pathologies in patients with epilepsy, we conducted a survey (a self-report questionnaire) to assess and compare the situation in patients with epilepsy and control subjects in terms of certain addiction domains, such as smoking, consuming alcohol, and using illicit drugs.

METHODS

One hundred and six patients with epilepsy aged between 18 and 65 years from an outpatient epilepsy clinic in a tertiary center comprised the study group. The control group composed of 96 age- and sex-matched subjects. Exclusion criteria for both groups were mental retardation, illiteracy, and having additional chronic systemic diseases, such as diabetes mellitus and hypertension.

The study population comprised any patient with epilepsy who visited our outpatient clinic during the survey. The names of the patients were written on the questionnaire to make necessary correlations with their clinical (age of epilepsy onset, duration and type of epilepsy, circadian feature of their seizures, and their response to treatment) and radiological data. Along with the patients, age- and sex-matched control subjects also took the survey. The control group included employees of an insurance company and the applicants or their relatives of a private psychology counseling center employees. All the participants were asked to answer the questions themselves.

The questionnaire was developed in our center as a self-report questionnaire. It comprised 20 questions that screened the three domains of addiction: smoking, consuming alcohol, and using illicit drugs (Table 1) as well as the demographic and socio-economic characteristics of the participants (age, gender, marital, educational, and financial statuses). Inquiry of addictive behaviors began with one or two qualifying questions investigating the presence of that particular domain. If the response to that question was "never/occasionally," those subjects were accepted as not addicted. If the response was "frequently/always," then they were compared for quantification. The questions were designed to interrogate the main elements of addiction, such as withdrawal, craving, and insight to dysfunction of interpersonal, social, and occupational relationships.

Statistical Analysis

This investigation was approved by our institutional ethics committee, and subjects provided informed consent. For statistical analyses, Number Cruncher Statistical System (NCSS; Utah, USA) 2007 statistical software was used. Descriptive statistical methods were used for calculation of mean values, standard deviation, percentages, and frequency distribution. Independent t-test was used for comparisons between the two groups, and chi-square test and Yates' correction was used for comparisons of qualitative data. $P < .05$ was considered as statistically significant.

RESULTS

Sociodemographic Results

Of all patients with epilepsy, 53% were male ($n=57$), and their mean age was found to be 32.66 ± 12.23 years. In the control group, 52% of the participants were male ($n=50$), and the mean age was found to be 35.70 ± 10.59 years. There was no statistically significant difference between groups regarding gender ($p=.810$) and mean ages ($p=.062$).

Mean age of epilepsy onset was 18.33 ± 13.23 (minimum: 1, maximum: 64) years. Mean duration of epilepsy was found to be 14.33 ± 11.26 (minimum: 1, maximum: 46) years. Majority of patients with epilepsy (84%) had focal epilepsy. The most common seizure types were focal seizures (46.2%) and secondarily generalized focal seizures (34.9%). Most of the patients had diurnal seizures; 64.2% ($n=68$) diurnal, 15.1% ($n=16$) nocturnal, and 20.8% ($n=22$) both. Majority of the patients (91.5%) had a normal neurological examination.

Nearly half of the patients (49.1%) had a normal cranial MRI. The lesions and their locations on cranial MR images are provided in Table 2. There were miscellaneous causes in six patients, such as multiple demyelinating lesions, giant aneurism, and lacunar infarcts. Four patients had heterotopia. Of these, one had a diffuse band heterotopia and the rest had nodular heterotopias located around the posterior horns of the lateral ventricles. Sequela lesions comprised post-traumatic, post-stroke lesions, or ischemic/gliotic lesions of unknown reasons. Out of the 16 patients, nine had left-sided mesial temporal sclerosis. Regarding the treatment response, 35.8% of the patients were in remission. The response to anti-epileptic treatment varied in the remaining group. Thirteen patients (five patients with mesial temporal sclerosis) had epilepsy surgery before the study period.

Concerning sociodemographic variables, there was a statistically significant difference between two groups with regard to marital status; there were more single people among patients with epilepsy ($p=.045$). The educational status between the groups did not reveal any statistical difference ($p=.064$). The ratio of being unemployed/house-wife was significantly 355

Table 1. The questionnaire for screening of smoking, consuming alcohol, and using illicit drugs

Choose the answer that describes you best by marking X in the box	Never	Occasionally	Often	Always
1. Do you smoke?	()	()	()	()
2. Do you smoke > 10 cigarettes daily?	()	()	()	()
3. Do you smoke in the morning before breakfast?	()	()	()	()
4. Does smoking prohibitions cause difficulty in your daily life?	()	()	()	()
5. Do you smoke when you had flu-like diseases?	()	()	()	()
6. Does smoking affect your social life?	()	()	()	()
7. To what extent do you use alcoholic beverages?	()	()	()	()
8. Do you drink >2 glasses of alcoholic beverage each time you start drinking?	()	()	()	()
9. Do you try to stop drinking because you think you drink too much of alcoholic beverages?	()	()	()	()
10. Have you ever required additional alcohol after a night of heavy drink?	()	()	()	()
11. Have any of your friends, a doctor, or a medical staff ever suggested you to stop consuming alcohol?	()	()	()	()
12. Have you ever used addictive drugs other than cigarette and alcohol?	()	()	()	()
13. Have you ever thought that substances you use may have caused addiction?	()	()	()	()
14. Do you have problems in withdrawing the substance you use?	()	()	()	()
15. Do your family and friends get annoyed regarding your consumption of tobacco and/or alcohol and/or substances?	()	()	()	()
16. Do you have problems in your family and/or in your business life because you use alcohol and/or substances?	()	()	()	()
17. Have you ever thought of illegally obtaining addictive substances?	()	()	()	()
18. Do you experience abstinence symptoms when you do not consume tobacco and/or alcohol and/or addictive substances? (such as, irritability, insomnia, fatigue)	()	()	()	()
19. Have you ever regretted after the use of alcoholic beverages and/or addictive substances?	()	()	()	()
20. Have you ever experienced amnesia on the following morning after a heavy drink and/or consumption of addictive drugs?	()	()	()	()

Table 2. Cerebral lesions of epilepsy patients and their locations on cranial magnetic resonance imaging

	MTS	C	D	H	S	Tm	M
Frontal					1		
Temporal	16	2			3	5	
Occipital					2		
Parietal			1			2	
Multilobar					11		6
Subcortical				4			
Number	16	2	1	4	17	8	6

MTS: mesial temporal sclerosis; C: cavernoma; D: dysplasia; H: heterotopia; S: sequeale lesions; Tm: tumor; M: miscellaneous causes

higher in the study group (p=.0001). Living with family was significantly more common among patients with epilepsy (p=.004). The comparisons of sociodemographic variables are shown in Table 3.

Results of Addictive Behaviors

Only alcohol consumption was found to be significantly lower in patients with epilepsy (p=.0001). Neither smoking (p=.530) nor using illicit drugs (p=.262) caused any significant difference between the groups (Table 4).

Regarding the disease period, smoking cigarettes was found to be less frequent in new onset epilepsies (<5 years) when compared with in epi-

or using illicit drug revealed no difference in terms of duration (p=.418, p=.321, respectively) (Table 4).

Having focal or generalized seizure did not cause any significant difference in rates of smoking, consuming alcohol, or using illicit drug (p=.628, p=.675, and p=.661, respectively). Furthermore, circadian feature of seizures (diurnal or nocturnal) did not cause any significant difference with respect to the aforementioned addiction domains (p=.137, p=.711, and p=.754, respectively) (Table 4).

Treatment response was categorized in three groups; being seizure free (35.8%, n=38), having daily seizures (11.3%, n=12), and others (52.9%, n=56). Treatment response and addiction domains did not reveal any statistically significant correlation (p=.801, p=.343, and p=.405, respectively).

With regard to etiological groups, patients with mesial temporal sclerosis on cranial MR images had no different attitudes from the rest of the group in all addictive domains (p=.459, p=.572, and p=.156, respectively).

DISCUSSION

Psychiatric comorbidities are frequently described in patients with epilepsy. When compared with some other chronic systemic diseases, such as diabetes mellitus, psychiatric symptoms are more frequently encountered in case of epilepsy, indicating a common substrate and pathogenesis in between psychiatric diseases and epilepsies.

Recent studies reveal that in case of epilepsy, which is now known as a network disorder, the involvement of dopamine-modulated basal ganglia

Table 3. Sociodemographic variables of study and control group

		Control group		Epilepsy group		
Age		35.70±10.59		32.66±12.23		t: 1.87 p=.062
Gender	Male	50	52.08%	57	53.77%	c ² : .06
	Female	46	47.92%	49	46.23%	p=.810
Marital status	Married	54	56.25%	48	45.28%	
	Single	36	37.50%	56	52.83%	c ² : 6.22
	Divorced	6	6.25%	2	1.89%	p=.045
Education	Elementary	18	18.75%	36	33.96%	
	8 years	17	17.71%	17	16.04%	
	11 years	26	27.08%	28	26.42%	c ² : 7.26
	11+ years	35	36.46%	25	23.58%	p=.064
Financial status	Student	8	8.51%	15	14.15%	
	Unemployed-housewife	5	5.32%	42	39.62%	
	Retired	26	27.66%	20	18.87%	
	1000-3000TL income	44	46.81%	26	24.53%	c ² : 40.67
	>3000 TL income	11	11.70%	3	2.83%	p=.0001
Chronic systemic diseases	No	85	88.54%	95	89.62%	c ² : .06
	Yes	11	11.46%	11	10.38%	p=.805
Who accompany at home	Alone	7	7.29%	0	.00%	
	Family	83	86.46%	104	98.11%	c ² : 10.89
	Friends	6	6.25%	2	1.89%	p=.004

TL: Turkish liras

Table 4. Results of addictive behaviors between the groups and within the study group

		Smoking % (n)					p value	Use of Alcohol % (n)					p value	Use of Illicit drug % (n)		
		Never	Sometimes	Often	Always	Never		Sometimes	Often	Always	Never	Sometimes		p value		
Whole group	Epilepsy group (n=106)	63.21 (67)	15.09 (16)	9.43 (10)	12.26 (13)	.530	80.19 (85)	19.81 (21)	-(0)	-(0)	.0001	99.06 (105)	.94 (1)	.262		
	Control group (n=96)	53.13 (51)	20.83 (20)	11.46 (11)	14.58 (14)		34.38 (33)	58.33 (56)	6.25 (6)	1.04 (1)		96.87 (93)	3.13 (3)			
Epilepsy duration*	<5 years (n=28)	46.40 (13)	32.10 (9)	14.30 (4)	7.10 (2)	.031	71.40 (20)	28.60 (8)	-	-	.418	100 (28)	-(0)	.321		
	≥5 years (n=76)	71.05 (54)	7.89 (6)	7.89 (6)	13.17 (10)		82.90 (63)	13.10 (13)	-	-		98.69 (75)	1.31 (1)			
Epilepsy type	Generalized (n=17)	64.70 (11)	5.90 (1)	11.80 (2)	17.60 (3)	.628	76.50 (13)	23.50 (14)	-(0)	-(0)	.675	100 (17)	-(0)	.661		
	Focal (n=89)	62.90 (56)	16.90 (15)	9.00 (8)	11.20 (10)		80.90 (72)	19.10 (17)	-(0)	-(0)		98.90 (88)	1.10 (1)			

*The epilepsy durations of two patients were not available.

circuits influencing thalamocortical projections may be a feature of both generalized and focal epilepsies (7). Moreover, it is shown in functional neuro-imaging studies that the meso-cortico-limbic system is activated in both drug and non-drug abusers (7). Therefore, it is of interest to evaluate addictive behavior in patients with epilepsy. To the best of our knowledge, there is no study regarding addictive behavior in epilepsies.

In our study, we found no statistical difference between the groups with respect to age and sex, although there were some differences in some sociodemographic variables, such as marital status, employment, and living with family. However, the control group may not be a representative group because some of them were office workers, meaning that they were already employed; this may create employment differences between the groups.

Addictive profiles of patients and the control group were different in terms of alcohol consumption probably implying the physician's role. Patients are usually recommended to avoid alcohol consumption because it triggers seizures and also interacts with the antiepileptic drugs. However, living with the family may also contribute to this difference because of their protective role over the patients.

The second important difference was the duration of epilepsy and frequency of smoking cigarettes. New onset epilepsy patients (<5 years) had lower smoking rates compared with patients of longer duration. This is the most important result because it may well indicate a psychiatric comorbidity, at least indirectly, in chronic epilepsy. However, in this study, we did not use an anxiety or depression scale to correlate addictive behaviors and the psychiatric comorbidities in patients with epilepsy that could verify this finding. Intractable and chronic epilepsies usually have a higher rate of psychiatric comorbidities; however, high-seizure frequency was not an indicator for any of the addictive domains in our study (8).

If prefrontal cortex and limbic cortex are the critical areas for addictive behavior; frontal and temporal lobe epilepsies may have a higher/lower risk for addictive behavior (3,4). It would be interesting to compare epilepsy groups according to the epileptogenic zone and evaluate their implications on addictive behavior. However, our sample comprised a heterogeneous epilepsy population. The origin of epileptic seizures was unclear in most of the patients. Although, a subgroup of patients with mesial temporal sclerosis on cranial MR images were chosen for comparisons with the rest of the patient population with regard to addictive behavior; this did not reveal any significant results. A further study in epilepsy surgery candidates in whom origin of the seizures are better clarified may justify this question.

The type and frequency of psychiatric comorbidity is reported to vary and increase in the post-surgical period, particularly in the refractory temporal lobe epilepsy. A certain part of these patients present with de novo post-surgical psychiatric problems that may cause more significant clinical problems than pre-surgery psychiatric problems. Considering overall post-surgical psychiatric comorbidities, various mechanisms are considered to be responsible for them, such as biological and neurochemical factors due to resection of certain areas of the limbic network, psychological factors such as the post-surgical expectations of the patient and their family, and also the patients' psychosocial adjustment to life afterwards (9). Therefore, we believe some interesting results could be observed if addictive behaviors were studied, particularly in the post-surgical period.

This study is designed as a cross-sectional study using a survey. Another limitation of our study may be the limited scope and effectiveness of the questionnaire that we designed ourselves. In Turkey, in 2012, occasionally or more frequently smoking above the age of 15 years was found to be 27% (10). Current alcohol consumption was found to be 25.6% in one population-based survey where the ages ranged between 12 and 65 years (11). Our sample size appears to be sufficient enough to detect any significance for smoking and consuming alcohol; however, we do not have the data regarding the use of illicit drugs in the population.

Epilepsy has more deleterious effects than any other chronic neurological diseases in terms of quality of life (QOL) mostly because of its unpredictable and episodic nature. It has both direct and indirect effects on QOL.

Its direct effects originates from its impact on domains such as physical and psychological health, whereas its indirect effects result from the limitations and restrictions it brings along as well as reducing the opportunities to engage in activities that contribute to QOL (12). Therefore, QOL is an important issue in patients with epilepsy. The major domains determining QOL in patients with epilepsy appear to be physical health, psychological or emotional health, social support, employment, and economic or material well-being (13). These domains may also contribute to the development of addictive behaviors. Therefore, addictive behaviors should be broadly evaluated in patients with epilepsy.

In this study, although there is not much difference between groups, further studies among homogeneous epilepsy subgroups with larger scale along with their neuropsychological profiles may still be confirmative in this subject.

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