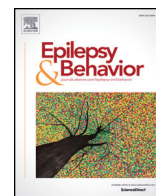




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Psychiatric comedication in patients with epilepsy

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ABSTRACT

Psychiatric disorders are more common in patients with epilepsy than in the general population. The aims of the study were to assess the frequency and type of psychotropic drug usage in patients with epilepsy, to assess the risk factors for their use, and to assess their proconvulsive potential and the risk of interactions with antiepileptic drugs. This 20-month prospective study included patients treated at the university hospital outpatient clinic. Psychotropic drugs have been classified according to the Anatomical Therapeutic Chemical Classification System. Of the 621 patients (with a mean age of 35.4 years), 60% were women, and 37.5% were in remission; 54.8% of the patients used antiepileptic drug monotherapy. The most commonly used antiepileptic drugs were valproate, levetiracetam, lamotrigine, and carbamazepine. Eighty-nine (14.3%) patients received psychiatric comedication. Sertraline, perazine, and hydroxyzine were the predominantly used psychotropic drugs. Independent variables associated with psychotropic drug usage in the logistic regression model included age, active epilepsy, combined focal and generalized epilepsy type, use of somatic comedication, and phenobarbital. Over one-third of the patients simultaneously received antiepileptic drugs and psychotropic drugs, between which clinically significant interactions may occur, 10% of patients used psychotropic drugs to lower the seizure threshold. The results of the study indicate the need for closer cooperation between doctors of various specialties when caring for patients with epilepsy.

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1. Introduction

Epilepsy is one of the most common chronic neurological diseases and occurs in nearly 1% of the population [1]. Many diseases occur in patients with epilepsy more often than in the general population. Mental disorders are of lifetime prevalence in up to 35% of patients with epilepsy [2], more often than in patients with other chronic diseases such as asthma or diabetes [3]. The most common mental disorders in patients with epilepsy include mood and anxiety disorders. Mental illnesses have a significant negative impact on the quality of life of patients with epilepsy, sometimes greater than the frequency of seizures [4]. However, they remain undiagnosed in many cases [5]. Pharmacotherapy tailored for psychiatric diseases is not used in all patients with epilepsy requiring treatment, and studies show even less frequent usage of psychotropic drugs than in the general population [6]. This results both from insufficient recognition of psychiatric conditions in patients with epilepsy as well as from the concerns of both neurologists and psychiatrists regarding the proconvulsive effect of psychotropic drugs and their interactions with antiepileptic drugs

(AEDs) [7,8]. Enzyme-inducing AEDs (carbamazepine, primidone, phenobarbital, and phenytoin) can significantly reduce the concentration and thus the effectiveness of many antidepressants and antipsychotics. Many psychotropic drugs, both old and new generation (including clomipramine, bupropion, and clozapine), lower the seizure threshold and may increase the frequency of seizures [9]. Knowledge of the above aspects of polytherapy is necessary in the case of simultaneous use of AEDs and psychotropic drugs for proper control of seizures and the effectiveness of psychiatric therapy.

Although numerous studies have so far been conducted on the prevalence of mental disorders in patients with epilepsy, the literature on their pharmacotherapy is insufficient [6,8,10].

The aims of this study were to assess the frequency and type of psychotropic drug use in patients with epilepsy, to assess the risk factors for their use, and to assess their proconvulsive potential and the risk of interactions with AEDs.

2. Materials and methods

2.1. Patients

The study included patients treated in the outpatient epilepsy clinic of the University Hospital in Krakow between 01/01/2016 and 08/31/2017.

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Participation in the study was proposed to patients diagnosed with epilepsy, as defined by the International League Against Epilepsy (ILAE) [11]. The study excluded patients who did not give their consent, patients with coexisting psychogenic nonepileptic seizures, and patients in which we failed to determine the type of epilepsy.

The protocol for the study followed the principles of the Helsinki Declaration and received approval from the bioethical committee of the Jagiellonian University of Krakow. Each patient was informed about the aim and methods of the study and gave their informed consent to participate.

2.2. Methods

Demographic and epilepsy data were collected using a structured questionnaire and included age, sex, age at onset of epilepsy, and type and frequency of seizures. Current antiepileptic medicines with their doses were reported. The type of epilepsy was diagnosed on the basis of interview, neurological examination, neuroimaging (magnetic resonance imaging or computed tomography, if magnetic resonance imaging was contraindicated), and electroencephalogram. Epilepsy type was classified according to the new ILAE position paper on the classification of epilepsies [12]. The studied group was divided into patients with focal epilepsy, generalized epilepsy (this group included patients with idiopathic (genetic) generalized epilepsies), and combined generalized and focal epilepsy. The last category consisted primarily of patients with the Lennox–Gastaut syndrome.

Data on the medicines used by patients were obtained in a prospective way from patient information obtained during two subsequent visits to the clinic. Patients were asked to bring the packaging of all drugs that they took on a regular basis and to provide information on their dosage. Psychotropic drugs were classified according to the Anatomical Therapeutic Chemical (ATC) Classification System [13]. All medicines used chronically by patients were reported. In this publication, psychotropic drugs from the following groups were considered: N05A antipsychotics, N05B anxiolytics, N05C hypnotics and sedatives, and N06A antidepressants. Benzodiazepines were classified as psychotropic drugs if they were not used as an antiepileptic medicine in an ad hoc or chronic manner.

The main author, who is the attending physician of all the patients included in the study, collected the following information: data on epilepsy and its medication from hospital records, data on psychotropic drugs from the hospital records, and documentation provided by the patients.

There was no verification of the psychiatric diagnosis for the purpose of this study.

The potential for interaction between antiepileptic and psychotropic drugs was evaluated on the basis of the Spina et al. study [14]. The following drugs were classified as causing a high risk of leading to a decline in the seizure threshold: antidepressants (amoxapine, bupropion, clomipramine, and maprotiline) based on Johannessen Landmark et al. [15] and antipsychotics (chlorpromazine, clozapine, and olanzapine) based on Pisani et al. [16].

2.3. Statistical analysis

Qualitative variables were presented by using numbers and percentages. Quantitative variables were described by using descriptive statistics: mean, median, standard deviation, minimum, and maximum. Significant differences between subgroups for quantitative variables were verified using the nonparametric U Mann–Whitney test. Verification of dependencies between categorical variables was calculated using the Pearson chi-square (χ^2) independence test. The significance of the differences between percentages for specific pairs of cases was verified using the significance test of differences for the structure index. The second part of the analysis included the analysis of the logistic regression model for factors that in the univariate analysis showed

the significance of differences between the group taking psychiatric drugs and that not taking such drugs. The model was created using backward stepwise regression. A significance level of 0.05 was assumed. Statistical analysis was performed using Statistica v. 12.5 (StatSoft Inc., Tulsa, OK, USA).

3. Results

3.1. Characteristics of the patient population

Six hundred twenty-one patients were enrolled in the study; 374 (60.2%) were women. The mean age of the respondents was 35.4 (SD = 13.6), and the average age at onset of epilepsy was 19.5 (SD = 14.5). Focal epilepsy was diagnosed in 466 (75.0%) patients, generalized (idiopathic generalized) in 135 (21.8%), and combined focal and generalized in 20 (3.2%). In 225 (36.2%) patients, seizures were frequent (>1 month) while 233 (37.6%) patients were in remission. Three hundred forty (54.8%) patients used monotherapy, and the most commonly used AEDs were valproate, levetiracetam, lamotrigine, and carbamazepine. Two hundred thirteen (34.3%) patients took at least one drug used in somatic diseases. The exact characteristics of the group in terms of frequency of seizures and pharmacotherapy of epilepsy are presented in Table 1.

3.2. The use of psychotropic drugs in patients with epilepsy

Eighty-nine (14.3%) patients were taking psychotropic drugs. The majority of patients in the latter group (62) took 1 drug, 16 patients took 2 drugs, 9 patients took 3 drugs, 1 patient used 4 drugs, and 1 patient used 5 psychotropic drugs. Fifty-six (9.1%) patients used antidepressants, 32 (5.1%) patients used antipsychotics, and 25 (4.0%) patients used anxiolytics, hypnotics, and sedatives. The most commonly used psychotropic drugs were sertraline (16 patients), perazine (11 patients), and hydroxyzine (10 patients). Table 2 presents the exact description of psychotropic drugs used by patients with epilepsy according to the ATC classification.

Table 1
Clinical characteristics of the study patients.

Variable	N = 621
Age [years]	35.4 (16–82)
Age at onset of epilepsy	19.5 (1–72)
Sex (women)	374 (60.2%)
Type of epilepsy	
Focal	466 (75.0%)
Genetic (idiopathic) generalized	135 (21.8%)
Combined focal and generalized	20 (3.1%)
Number of AEDs used	
1	340 (54.8%)
2	204 (32.8%)
3	71 (11.4%)
4	6 (1.0%)
Seizure frequency	
More than 1 per month	225 (36.2%)
Less than 1 per month, more than 1 per year	163 (26.2%)
Less than 1 per year	233 (37.6%)
The most commonly used AEDs (in mono- or polytherapy)	
Valproate	310
Levetiracetam	209
Lamotrigine	136
Carbamazepine	125
Topiramate	66
Oxcarbazepine	49
Clonazepam	26
Lacosamide	23
Gabapentin	13
Phenobarbital	9
Drugs used in somatic diseases	213 (34.3%)

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