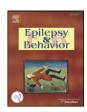
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Determinants of quality of life in people with epilepsy in Serbia

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ABSTRACT

Purpose: This study aimed at finding determinants of quality of life in people with epilepsy (PWE) living in Belgrade. Serbia.

Method: In this study, we recruited consecutive adults with epilepsy attending our outpatient department. Adult patients (age range: 18–65 years) of normal intelligence and without any progressive neurological disease or psychiatric disorder were included in the study. They completed the following questionnaires: QOLIE-31 Inventory (Serbian version), Beck's Depression Inventory-II, Beck's Anxiety Inventory, Symptom Check List-90, and Neurotoxicity Scale-II. Hierarchical multiple regression analysis was performed to assess the predictive effects of some factors on QOLIE-31 Inventory.

Results: The mean QOLIE-31 score of 203 patients who completed the questionnaires was 70.64 ± 17.74 . Sociodemographic factors (age, sex, education, and employment) did not significantly predict QOLIE-31 score. Significant determinants of quality of life were clinical characteristics – seizure severity and etiology of epilepsy – accounting for 30.9% of the variance, depressive and anxiety symptoms accounting for 42.8% of the variance, and cognitive effects of antiepileptic drugs, accounting for 1.5% above other variables.

Conclusions: The results suggest that seizure severity and etiology of epilepsy, depressive and anxiety symptoms, and cognitive adverse medication effects are main determinants of quality of life in this population of PWE.

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1. Introduction

Epilepsy is often associated with high rates of psychiatric comorbidity, impaired cognitive development, and other important psychosocial consequences, such as driving and employment restrictions. In line with these facts, previous researchers revealed that health-related quality of life (HRQOL) in people with epilepsy (PWE) has multiple determinants, which include not only the aspects specific to the condition (such as the impact of seizures and adverse effects of antiepileptic drugs) or psychiatric comorbidities but also sociocultural and environmental factors (for recent reviews, see Jacoby et al. [1] and Taylor et al. [2]).

However, a majority of studies searching for predictors of HRQOL in epilepsy have been conducted in heterogeneous populations of patients and often focused on highly selected populations, such as patients on monotherapy [3], subjects with epilepsy pharmacoresistant to antiepileptic drugs (AEDs) [4], patients with drug-refractory epilepsy undergoing surgery [5,6], subjects with temporal lobe epilepsy [7], and ethnic minorities [8], or the impact of seizures and adverse effects of treatment [9–11] or seizures and comorbidities, particularly anxiety and depression [12–17]. Recently, several studies have addressed comprehensively

the relative contribution of demographic, disease-related, and treatment-related variables in people with epilepsy [4,12,18–21].

In spite of reliable and valid assessment tools and methodology used in these studies, differences in the predictive influence of various factors still persisted. A recent review [2] concluded that the evidence for predictive influence of educational and employment status was conflicting. The relative contribution of anxiety and depressive symptoms differed in various studies. One probable cause for the mentioned discrepancies in findings may be considerable differences in sociocultural and environmental factors, service provision, social milieu, and attitudes in various countries, which preclude the extrapolation of the findings obtained in one population to other patient groups or other regions [1]. Although the quality of life (QOL) in various populations of PWE living in different sociocultural milieus seems to be quite different, there are several QOL predictors, for example, seizure severity and psychiatric comorbidities, which are consistent among studies from all over the world, and those that are divergent, such as the effect of seizure frequency [9,18,22], polytherapy [12–15], or gender [3]. Therefore, our purpose was to define precisely the relative contributions of QOL predictors in people with epilepsy living in Serbia. The obtained results may be useful in planning health services, resource allocation, and other measures aiming to improve the QOL in our population of PWE.

In our previous study [22], we have validated the Serbian adaptation of the QOLIE-31 (Quality of Life in Epilepsy Inventory) [23] and found that epilepsy-related factors (seizure severity and etiology of epilepsy)

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influenced all domains of QOLIE-31 except the medication effect scale. Since QOLIE-31 includes a wide spectrum of concerns facing people with epilepsy (PWE), the aim of the present study was to define the predictive value of sociodemographic characteristics, clinical factors, depression and anxiety symptoms, and cognitive adverse effects of AEDs on QOL scores in a sample of adult PWE in Serbia.

2. Patients and methods

2.1. Participants

All adult patients who attended regular appointments at the Department of Epilepsy and Clinical Neurophysiology of The Institute of Mental Health in Belgrade were enrolled consecutively in the study. People with epilepsy aged 18–65 years with a diagnosis of epilepsy made by neurologists according to the criteria of the 2001 International Classification of Epilepsies and Epileptic Syndromes (ILAE) [24] were eligible if they were able to understand and complete the questionnaires. All subjects gave informed consent before their inclusion in the study. Exclusion criteria were as follows: presence of a significant psychiatric disorder requiring the use of antipsychotic drugs, progressive neurological disease, and concomitant use of neuroleptic drugs, cranial trauma, or craniotomy during the last year. The study was approved by the Ethical Committee of the Medical School, the University of Belgrade.

2.2. Instruments

Sociodemographic data (age, educational level, occupational status, and marital status) were obtained by using a semistructured interview. Clinical characteristics of epilepsy including details on epilepsy history, seizure types and seizure frequency, comorbidities, and drug treatment were obtained from the medical records of patients. Seizure severity groups were defined according to a composite measure that includes both type and frequency of seizures. The severity of seizures and their clinical manifestations (e.g., automatisms) may have equal or greater impact on patient well-being than the total number of seizures. An example is the reduction in severity from secondarily generalized tonic-clonic seizures (GTCSs) to complex partial seizures (CPSs) and from CPSs with altered consciousness to simple partial seizures (SPSs) with consciousness maintained. If the postictal period is shortened, the patients can resume activities rapidly [25]. Controlled epilepsy was the term used if the patient was seizure-free in the last 12 months.

Subjects completed five self-report measures: (1) the Serbian translation of the QOLIE-31 [22] used in the original report by Cramer et al. [23], (2) the Beck's Depression Inventory-II [26], (3) the Beck's Anxiety Inventory [27], (4) the Symptom Check List-90 [28], and (5) the Neurotoxicity Scale-II [29].

We used the Serbian version of QOLIE-31 that was validated previously on the same sample, showing satisfactory psychometric properties — good reliability, high internal consistency, and a high degree of conceptual similarity to the original American version [22].

Mood was assessed by using the Beck Depression Inventory, revision II (BDI-II), a 21-item self-report measure of the severity of depressive symptoms. Each item was scored from 0 to 4, with higher scores indicating more severe symptoms. The BDI total score was categorized using cut-off points (0-9 = normal; 10-18 = mild to moderate depression; 19-29 = moderate to severe depression; above 29 = severe depression) [26].

The Beck Anxiety Inventory (BAI) [27] is a self-report scale which has 21 multiple-choice questions that are scored from 0 to 4. Anxiety symptoms are quantified in four categories with the same cut-off points as for the BDI-II.

The Symptom Checklist-90—Revised (SCL-90-R) [28] is a 90-item self-report inventory designed to assess current psychological symptoms in community, medical, and psychiatric settings. From the SCL-90-R, which was demonstrated to be sensitive to change among

individuals with epilepsy [30], the standardized scores (gender-corrected) of two subscales were used for this study. Although both the BDI-II scale and SCL-90-R depression subscale measure the same characteristics, we decided to use both instruments in order to compare their relations with QOLIE-31. An equivalent rationale justified the use of both BAI-II and SCL-90-R anxiety scales in this study.

The Neurotoxicity Scale-II (NTS-II) was devised as a patient self-report scale to assess the adverse effects of antiepileptic drugs on cognitive function [29] in six cognitive domains comprising fatigue, slowing, memory, concentration, motor coordination, and language. The overall score, ranging from 0 to 72, is the most valid primary outcome measure, which indicates whether a subject had experienced cognitive impairment and associated it with the AED treatment.

2.3. Statistical analysis

The Kruskal–Wallis test was used to determine differences of NTS-II score between patients receiving monotherapy, two, or three drugs. Pearson's correlation coefficient and canonical correlation analysis were performed to assess the correlations between QOLIE-31 overall and subscale scores and BDI-II, BAI, SCL-90-R, and Neurotoxicity Scale-II scores.

Multiple regression, using enter method, as well as hierarchical multiple regression were used to assess the predictive value of different variables on QOLIE-31 scores.

The hierarchical multiple regression analysis was used after a determination of R^2 and the partial coefficients of each variable at the point at which it is added to the equation [31]. For all analyses, the dependent variable was QOLIE-31 overall score. For statistical analysis we used statistical package PASW Statistics 18.

3. Results

3.1. Clinical characteristics and self-assessment questionnaires

Table 1 presents the demographic, disease-related, and treatment-related characteristics of the study population and the results of self-assessment questionnaires. The mean age was 37.9 years (range: 18–65), and the mean duration of epilepsy was 18.6 years. All patients were white non-Hispanic Caucasians. There was no ethnic or racial heterogeneity in the sample population. Educational level of 157 (77.4%) patients was either low with completed elementary school or intermediate with completion of high school. Severity of seizures was low in almost one-half of the patients. All subjects received antiepileptic drug treatment, and 113 (55.6%) patients were on polytherapy.

Mean total QOLIE-31 score (SD) was 70.64 (17.74); subscale scores are presented in Table 1. According to BDI-II, 67 (33%) patients had symptoms of depression (score above 9), and the mean depression score on SCL-90 was 9.05. Beck Anxiety Inventory scores above 9 (suggesting an anxiety disorder) were recorded in 73 (36%) patients, while the mean anxiety score on SCL-90 was 6.08. Mean NTS-II scores were significantly higher in patients receiving three drugs (27.44) in comparison with patients receiving monotherapy (9.27) (Kruskal–Wallis $\chi^2=17.314$; p = 0.002).

3.2. Predictors of quality of life

Regression analysis showed a significant correlation between depression measures (BDI-II and SCL-90 depression scores) and total QOLIE-31 score (Fig. 1). These measures predicted 64% of quality-of-life score (F = 51.88, p < 0,001, $R^2 = 0.636$). Total QOLIE-31 score was highly significantly correlated with both depression measures (rho = 0.836), but the value was higher for BDI-II (-0.975) than for SCL-90 (-0.845) scores. According to the tests of regression coefficients, the BDI-II score was a significant measure for prediction of QOLIE-31 ($\beta = -0.55$, t = -5.17, p < 0,001). The canonical

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