

Research Article**Antiepileptic drugs and quality of life in patients with epilepsy: A tertiary care hospital-based study****Rizaldy Taslim Pinzon, Fransiscus Buwana, Rosa De Lima Renita Sanyasi, Andre Dharmawan Wijono, Jesisca***Faculty of Medicine Duta Wacana Christian University, Yogyakarta, Indonesia*

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Abstract

Background: Epilepsy rates are still high in developing countries, particularly in the case of Indonesia. It becomes big problem since it often leads to the risk of social discrimination/isolation, fear and social stigma. In spite of that, giving a proper treatment to patients with Epilepsy may help them to manage the epilepsy and improve the life quality of the patient. **Objective:** The present study evaluated patterns of the use of anti-epileptic drugs (AEDs) and their impact on quality of life (QOL) in patients with epilepsy. **Materials and Methods:** In this cross sectional study, the subjects were epileptic patients ≥ 18 years of age who were diagnosed with epilepsy in Neurological Outpatient Clinic Bethesda Hospital. Demographic, clinical and treatment parameters were recorded. The evaluated outcome was the value of adjusted SF-8 Questionnaire. **Results:** From 29 patients, 51.72% were males and 58.62% were younger than 60 years. Seizures were predominantly general (89.65%) and partial (10.34%). Patients with immediate therapy were more often found than the delayed therapy (79.31% vs. 20.69%). Patient with delayed therapy have low general health score (40.56 ± 9.07). Twenty six (89.65%) were on monotherapy, two were on two drugs (6.89%) and one patients received more than two drugs (3.44%). Patients with more than one drugs have low general health score (42.70 ± 14.33). Most patients got therapy less than 18 year (96.55% vs. 1.03%). Patient who got therapy more than 18 years have low general health score (32.56). **Conclusion:** Patients got immediate therapy, monotherapy anti-epileptic drugs and less than 18 years have a better quality of life.

Keywords: epilepsy, anti-epileptic drugs, quality of life

Introduction

Epilepsy is one of the common neurological disorders, which require immediate medical attention and long-term therapy (Pimpalkhute et al., 2015). Epilepsy can be diagnosed at any age and is associated with increased risk of premature death (Gilmour et al., 2016). World Health Statistics (2018) has reported more than 50 million people worldwide have epilepsy and nearly 80% of the people with epilepsy live in low- and middle-income countries.

The burden of epilepsy may be due to psychological and social, such as the negative attitudes of people towards the patients, manifested as social stigma, social isolation and lack of support (Mula et al., 2016; Dogan et al., 2015). Furthermore, it can lead

to low self esteem, depression, anxiety, negative feelings, impaired social skills and their impact on quality of life (Heersink et al., 2015). Such growing recognition of the importance of the psychosocial effects of epilepsy has led to the need to quantify QOL in affected individuals (George et al., 2015).

There are several studies examining the quality of life (QOL) of epileptic patients worldwide. In a study conducted Clinic of Neurology, Sri Venkateswara Institute of Medical Sciences, India showed polytherapy is associated with poor QOL (Nagarathnam et al., 2017). Immediate antiseizure drug treatment reduces the risk of seizure recurrence over the next one to two years (Marson et al., 2005). In spite of that, giving a proper anti-epileptic drug (AED) and assessment of QOL as an outcome measure are important in the management of epilepsy to achieve optimal seizure control (Pimpalkhute et al., 2015; George et al., 2015).

Very few studies have been carried out about anti-epileptic

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drugs and quality of life in Indonesia. The aim of this study was to evaluate patterns of the use of anti-epileptic drugs (AEDs) and their impact on quality of life (QOL) in patients with epilepsy.

Materials and methods

Study design and sampling

This was a cross-sectional, questionnaire-based study conducted between November to Desember 2017 at the Neurology Outpatient Department of Bethesda Hospital, Yogyakarta, Indonesia. Patient with epilepsy aged 18 years or older and consenting to participate were included in the study following a written informed consent. Patients aged less than 18 years or not to participate were excluded from the study. The epilepsy was diagnosed with standard way by well-trained neurologist and confirmed with EEG. We used consecutive sampling to collecting all participants. A random sample of 29 patients who met the inclusion criteria was recruited, which was deemed adequate to detect a clinically meaningful difference in QOL scores.

Questionnaires were developed to collect socio-demographic (sex, age, education level, employment status) and clinical aspects of epilepsy (family history of epilepsy, history of status epilepticus, aetiology, neuroimaging, EEG test, type of seizure, starting of AED, duration of AED, number of AED).

We divide starting of AED into 2 group; immediate therapy and delayed therapy. The main calculated predicting factors were the patients with immediate therapy (<10 attacks seizure) and delayed therapy (≥ 10 attacks seizure) (Pinzon et al., 2003). Duration of AED divide into 2 group; duration therapy ≤ 18 years and >18 years (Djibuti et al., 2003). Number of AED divide into 2 group monotherapy (single drug treatment) and polytherapy (more than one drug treatment) (Deckers et al., 2001).

Quality of life

The evaluated outcome was the value of adjusted SF-8 Questionnaire. The SF-8 Health Survey is the most recent version of the (Short Form) health surveys, which are the most widely used patient based health surveys in the world. We take the questioner from Optum™. SF-8 questionnaire consisting 8 subscales, including: Physical Functioning (PF), Role Physical (RP), Body Pain (BP), General Health (GH), Vitality, Social Functioning (SF), Role Emotional (RE), Mental Health (MH) and 2 subscales for summary including: Physical Component Score (PCS), Mental Component Score (MCS). The overall score ranged from 0 to 100, with higher scores representing better QOL.

Ethical approval

Ethical clearance was obtained from the institutional ethics clearance committee, Faculty of Medicine Duta Wacana Christian University, Yogyakarta, Indonesia. The Number for ethical clearance is 583/C.16/FK/2018.

Statistical Analysis

Statistical analyses were performed using Statistical Package for Social Sciences (SPSS) for Windows version 20.0. Mean and standard deviation for each of the demographic, epilepsy data, and the QOL scores were calculated. One-way analysis of variance (ANOVA) was used to test the difference between groups to evaluate whether the means were significantly different from each other. Two-tailed "P" values below 0.05 were considered significant.

Results

Sosio-demographic and clinical characteristics

A Total of 29 patients who were recruited into the study fulfilled the eligibility criteria. The majority were males (51.72%) and 58.62% were younger than 60 years. 28 respondents had formal education while 1 were not educated. Majority of patients were also employed (68.96%) and most of epilepsy patients had no family history of epilepsy (89.65%).

Table 1. Socio-demographic and clinical profile of patients with epilepsy

Parameters	Category	N (%)
Sex	Male	15 (51.72)
	Female	14 (48.28)
Age	<60 years	17 (58.62)
	>60 years	12 (41.37)
Education	Not educated	1 (3.44)
	Elementary school	4 (13.79)
	Junior high school	4 (13.79)
	Senior high school	11 (37.93)
	Bachelor	9 (31.03)
Employment	Unemployed	9 (31.03)
	Employed	20 (68.96)
Family history of epilepsy	Yes	3 (10.34)
	No	26 (89.65)
History of status epilepticus	Yes	3 (10.34)
	No	26 (89.65)
Aetiology	Idhiopathic/unkown	10 (34.48)
	CVA	19 (65.51)
Neuroimaging	Normal	10 (34.48)
	CVA	19 (65.51)
EEG test	Normal	3 (10.34)
	Abnormal	26 (89.65)
Type of seizure	Generalized seizure	26 (89.65)
	Partial seizure	3 (10.34)
Starting of AED	Immediate	23 (79.31)
	Delayed	6 (20.68)
Duration of AED	≤ 18 years	28 (96.55)
	>18 years	1 (3.44)
Number of AED	Monotherapy	26 (89.65)
	Polytherapy	3 (10.34)

CVA: Cerebrovascular Accident, EEG: Electroencephalography, AED: Anti Epileptic drug

Table 2. QOL of patients with immediate therapy and delayed therapy

Parameters	Immediate therapy	Delayed therapy	P-value
Physical Functioning	45.68±9.32	44.48±9.35	0.715
Role Physical	46.59±8.32	46.17±9.40	0.909
Body Pain	51.97±8.02	46.05±8.11	0.107
General Health	44.45±6.73	40.56±9.07	0.303
Vitality	51.74±9.66	51.37±12.90	0.539
Social Functioning	47.24±8.41	43.74±13.74	0.653
Role Emotional	44.32±7.26	42.31±11.53	0.844
Mental Health	48.39±8.23	43.10±13.53	0.391
Physical Component Score	47.27±8.61	45.51±4.49	0.451
Mental Component Score	47.93±9.32	43.35±13.42	0.628

Table 3. QOL patients with monotherapy and polytherapy

Parameters	Monotherapy	Polytherapy	P-value
Physical Functioning	45.41±9.61	44.20±5.84	0.864
Role Physical	46.77±8.72	42.82±5.80	0.578
Body Pain	50.60±8.46	47.67±0.00	0.454
General Health	43.92±7.05	42.70±14.33	0.705
Vitality	49.60±10.39	49.50±11.87	0.779
Social Functioning	46.87±9.94	44.94±6.40	0.544
Role Emotional	43.73±8.33	49.04±4.78	0.476
Mental Health	46.75±9.86	45.04±4.78	0.410
Physical Component Score	47.14±8.09	43.31±8.98	0.740
Mental Component Score	46.45±10.62	45.04±4.61	0.636

Type of seizure was generalized in 26 (89.65%), partial in 3(10.34%). The major attributable etiologies for seizure was cerebrovascular accident (65.51%) and 10 (34.48%) patients had an idiopathic or cryptogenic origin for seizures.

Twenty six (89.65%) were on monotherapy, two were on two drugs (6.89%) and one patients received more than two drugs (3.44%). Most patients got immediate therapy (79,31%) and duration of treatment less than 18 year (96.55%).

Patients with immediate therapy had better overall scores than patients with delayed therapy. Among epilepsy patient with immediate therapy, the lowest and the highest mean scores were found for role emotional (44.32±7.26) and body pain (51.97±8.02) subscales. In group consisted of patients with delayed therapy, general health (40.56±9.07) had the lowest mean scores and vitality (51.37±12.90) had the highest mean scores. However, these differences were not statistically significant.

Patients with monotherapy therapy had better overall scores than patients with polytherapy. Among epilepsy patient with monotherapy therapy, the lowest and the highest mean scores were found for role emotional (43.73±8.33) and body pain (50.60±8.46) subscales. In group consisted of patients with polytherapy, general health (42.70±14.33) had the lowest mean scores and vitality (49.50±11.87) had the highest mean scores. However, these differences were not statistically significant.

Patients with duration therapy ≤18 years had better overall scores than patients with >18 years therapy. Among epilepsy patient with duration therapy ≤18 years, the lowest and the highest mean scores were found for role emotional (43.84±8.26) and body pain (50.85±8.39) subscales. In group consisted of patients with duration therapy >18 years, general health (32.56) had the lowest mean scores and vitality (47.67) had the highest mean scores. However, these differences were not statistically significant.

Tabel 4. QOL of patients with duration of treatment

Parameters	Duration ≤18 years	Duration >18 years	P-value
Physical Functioning	45.62±9.28	40.07	0.417
Role Physical	46.78±8.40	38.71	0.255
Body Pain	50.85±8.39	47.67	0.753
General Health	44.04±7.07	32.56	0.113
Vitality	50.25±10.32	45.16	0.495
Social Functioning	46.73±9.66	40.41	0.382
Role Emotional	43.84±8.26	43.66	0.950
Mental Health	47.21±9.69	46.59	1.000
Physical Component Score	47.26±7.80	36.96	0.188
Mental Component Score	46.92±10.38	45.77	0.905

Discussion

The ultimate goal of epilepsy treatment is no seizures and no adverse effects with an optimal QOL. Adopting evaluation of QOL outcomes in the standard management plan along with traditional measures of assessment of seizure frequency and adverse effects is hence increasingly encouraged (Perucca et al., 2011). To address this objective, the present study examined patterns of AED use and their influence on QOL in patient with epilepsy.

The decision of whether or not to start antiseizure drug therapy at the time of a first unprovoked seizure in an adult should be individualized based on a discussion of the risk of seizure recurrence, the effectiveness of anticonvulsant treatment, and the adverse medical and socioeconomic effects of anticonvulsant treatment (Ibrahim and Benbadis, 2018). Immediate antiseizure drug treatment reduces the risk of seizure recurrence over the next one to two years (Marson et al., 2005). This estimate is derived from a meta-analysis of five randomized trials (n = 1600 patients) comparing immediate versus delayed antiseizure drug therapy in adults with an unprovoked first seizure (Krumholz et al., 2015).

Our study compare immediate vs delayed antiseizure drug therapy in patients with few or infrequent seizures on quality of life (QOL) outcomes. Patients with immediate treatment had better overall scores than patients with delayed treatment. Patients with delayed treatment had low physical functioning, role physical, body pain, general health, social functioning, mental health. However, these differences were not statistically significant. Previous study showed that there were no significant differences in QOL outcomes both patient with immediate and delayed treatment (Jacoby et al., 2007). Immediate treatment did not contribute to the overall mortality of epilepsy after the first seizure (high quality evidence), but treatment of the first seizure

was associated with a significantly higher risk of adverse events and impact on quality of life outcomes (Leone et al., 2016; Micoulaud et al., 2017).

In recent years, numerous studies have proved improved QOL with monotherapy (Sureka et al., 2017; Auriel et al., 2009; George et al., 2015). This may be partly due to reduced adverse effects commonly associated with polytherapy. Patient with polytherapy have adverse event such as difficulty in concentrating, vertigo, disturbed sleep, depression, nervousness/agitation and drowsiness (Joshi et al., 2017). The QOL was evaluated in relation to number of drugs in the present study and was found that patients on polytherapy had lower QOL scores compared to patients on single drug. This difference between monotherapy and polytherapy scores did not show any statistical significance, but patients with monotherapy therapy had higher overall scores than patients with polytherapy. On this study patients with polytherapy had poor physical functioning, role physical, body pain, general health, social functioning, mental health. This finding is in agreement with previous study which showed polytherapy is associated with poor QOL (Nagarathnam et al., 2017; Nabukenya et al., 2014; Alexander et al., 2018).

As a general rule, adult patients should have been seizure-free for at least two years before discontinuation is considered. In children with epilepsy where the prognosis is known to be good, discontinuation may be considered earlier (Lossius et al., 2017). Patients with long-term antiepileptic drugs have failed to produce seizures control (Kenneth et al., 2014). On the other side, more than half of those who use antiepileptic drugs report adverse effects and many are concerned about these effects in the long-term (Perucca and Gilliam, 2012). Patients with uncontrolled seizures and have adverse events of antiepileptic drugs

negatively impact quality of life (George et al., 2015). On our study, patients with duration therapy >18 years had worse overall scores of quality of life than patients with ≤ 18 years therapy. Patients with duration treatment more than 18 years had poor physical functioning, role physical, role emotional, body pain, general health, social functioning, mental health.

Conclusion

Patients got immediate therapy, monotherapy anti-epileptic drugs and less than 18 years have a better quality of life. Giving a proper treatment to patients with epilepsy may help them to manage the epilepsy and improve the life quality of the patient.

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Conflict of Interest: None declared.

Authors Contribution

Rizaldy Taslim Pinzon: Concept and design of the study, manuscript preparation, statistically analyzed and interpreted, critical revision of the manuscript.

Fransiscus Buwana: Concept and design of the study, collected data, preparing first draft of manuscript, critical revision of manuscript, review of the study and reviewed the literature.

Rosa De Lima Renita Sanyasi: Concept and design of the study, collected data

Andre Dharmawan Wijono: Concept and design of the study, collected data

Jesisca: Concept and design of the study, collected data

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