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Antiepileptic Drugs and Quality of Life in Patients with Epilepsy: A Tertiary Care Hospital-Based Study

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ABSTRACT

Objectives: The present study evaluated patterns of the use of antiepileptic drugs (AEDs) and their impact on quality of life (QOL) in patients with epilepsy. **Methods:** In this cross-sectional study, patients with epilepsy (age >18 years) receiving AEDs for at least 1 year were enrolled. Demographic, clinical, and treatment parameters were recorded. QOL was measured using the modified Quality of Life in Epilepsy Inventory-10 (QOLIE-10) questionnaire for epilepsy. **Results:** Of 200 patients, 53.5% were males and 60% were younger than 30 years. Seizures were predominantly partial (58%) and of idiopathic origin (61%). Monotherapy to polytherapy ratio was 1:1, with 70% of the patients on one new AED. Clobazam (37%) was used most frequently followed by phenytoin (25.5%), levetiracetam (23%), oxcarbazepine (21.5%), and carbamazepine (21%). Patients on polytherapy experienced a significantly more number of adverse drug reactions than did those on monotherapy ($P < 0.0001$). The mean QOLIE-10 score was 74.58 ± 20.60. There was no significant difference in seizure frequency, number of adverse drug reactions, and QOLIE-10 score among patients receiving old and new AEDs. Multiple linear regression analysis identified increased seizure frequency (standardized β −0.157; $P = 0.003$), more number of AEDs (standardized β 0.107; $P = 0.05$) as well as adverse drug reactions (standardized β −0.692; $P = 0.0001$) as significant predictors of poor QOL. **Conclusions:** Appropriate tools for early detection, selection of rational and safer AED treatment options, and regular monitoring for adverse effects play a crucial role in achieving seizure freedom and optimal QOL in patients with epilepsy.

Keywords: antiepileptic drugs (AEDs), epilepsy, quality of life (QOL).

Introduction

Epilepsy, the second most common neurological condition after headache, is characterized by recurrent seizures of cerebral origin. Fifty million people in the world and an estimated 6 to 10 million people in India suffer from epilepsy [1–3]. It is of concern that the diagnosis and management of epilepsy is often suboptimal in developing countries and in the European region [4,5].

Epilepsy is both a medical diagnosis and a social label [6] because people with epilepsy face many psychosocial challenges (anxiety, social stigma, difficulty in driving, unemployment) that can negatively impact quality of life (QOL). Such growing recognition of the importance of the psychosocial effects of epilepsy has led to the need to quantify QOL in affected individuals. Hence, appropriate antiepileptic drug (AED) use, along with monitoring of adverse effects, and assessment of QOL as an outcome measure are important in the management of epilepsy to achieve optimal seizure control.

The measurement of QOL using validated tools such as Quality of Life in Epilepsy Inventory-31 [7], Quality of Life in Epilepsy Inventory-10 (QOLIE-10) [8], and short-form 36 health survey [9] are popular. The evaluation of QOL is a relatively new measure to assess patient-related outcome of AED treatment for epilepsy. Demographic characteristics, high seizure frequency, and long duration of the disorder have been shown to correlate strongly with poor QOL [10]. Although several new AEDs have been licensed over the last decade, there are limited numbers of studies that have examined the impact of AED pharmacotherapy (type of AED/monotherapy, polytherapy/adverse drug reactions [ADRs]) on QOL [4].

The present study was designed to evaluate patterns of AED use and to examine the impact of factors, namely, demographic, clinical, and pharmacotherapy characteristics, affecting QOL.

Methods

Study Design and Sampling

This was a cross-sectional study conducted over 15 months (January 2011–March 2012) at the Neurology Outpatient Department of St. John's Medical College, Bangalore, India. Institutional Ethical Review Board approval was obtained. To be powered at 90% with 5% alpha error, 92 patients were needed for the study to detect a difference of 10 SD in QOL scores between patients on AED monotherapy and polytherapy. A random sample of 200

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Table 1 – Sociodemographic profile of patients with epilepsy.

Parameters	Category	N = 200, n (%)
Sex	Male	107 (53.5)
	Female	93 (46.5)
Age (y)	Mean age ± SD/ median	31.46 ± 12.834/26
Marital status	Married	118 (59)
	Unmarried	82 (41)
Residence	Urban	115 (57.5)
	Semiurban	62 (31)
	Rural	23 (11.5)
Education	Primary school and below	40 (20)
	High school to PUC	94 (47)
	Degree and professionals	66 (33)
Employment	Employed	96 (48)
	Unemployed	72 (36)
	Student	32 (16)
Per-capita income (INR)	10,000–50,000	69 (34.5)
	>50,000	5 (2.5)

INR, Indian rupee; PUC, pre-university college.

patients who met the inclusion criteria was recruited, which was deemed adequate to detect a clinically meaningful difference in QOL scores (10–11 points) across other variables [11].

Selection Criteria and Data Collection

Patients with epilepsy (PWE) aged 18 years or older receiving AEDs for at least 1 year and consenting to participate were included. The International League Against Epilepsy classification of seizures and epileptic syndromes was followed [12]. Patients with significant disability, major psychiatric disorders, severe medical comorbidity confounding QOL assessment, and an AED change in the last 1 month were excluded.

A structured case record form was used to collect data on sociodemographic, clinical, and treatment parameters. Seizure burden was scored according to the Engel system [13] for seizure frequency and burden in a quasi-logarithmic scale ranging from 0 to 12. Scores less than 5 were considered as no seizures. A score of 5 denotes one to three seizures per year, and a score of 6 indicates 4 to 11 seizures per year. Seizure frequency of one per month was scored as 7 to 12. Persons were said to be seizure free if there was absence of disabling seizures for more than 12 months. Treatment data included generic names, daily dose, duration, and adverse reaction profile after the administration of AEDs.

The QOLIE-10, an abbreviated questionnaire consisting seven domains and 10 items derived from the QOLIE-31, was used to assess QOL [8,14]. The overall score ranged from 0 to 100, with higher scores representing better QOL. We used the English version of the QOLIE-10, and the question on driving was modified to suit the Indian scenario. Patients conversant in English completed the questionnaire, and the remaining patients in the multilingual patient population were explained the questions in their respective languages and responses were recorded.

Statistical Analysis

Data were analyzed using SPSS version 20. Descriptive data were expressed as mean ± SD, median, interquartile range, and percentages. The QOLIE-10 scores were expressed as mean ± SD with 95% confidence intervals. Categorical variables were compared using the chi-square test. Continuous variables were analyzed using the unpaired *t* test and analysis of variance (parametric), the Mann-Whitney *U* test, the Kruskal-Wallis test (nonparametric), and the Spearman correlation coefficient. The significant variables in univariate analysis were entered into a stepwise multiple linear regression model to identify the significant predictors of poor QOL. Statistical significance was set at $P < 0.05$.

Results

Demographic and Clinical Characteristics

A total of 200 patients who were recruited into the study fulfilled the eligibility criteria. The majority were males (53.5%) and 60% of patients were between 18-30 years. Type of seizure was partial in 116 (58%), generalized in 84 (42%), and 122 (61%) patients had an idiopathic or cryptogenic origin for seizures. The common attributable etiologies for seizures were central nervous system infections (neurocysticercosis), vascular, degenerative disorders, and head injury. Median age at onset of epilepsy was 18 years and duration was 7.5 years. Seizure frequency was one to three per year (Engel score 5) in 47% of the patients, and 30% were seizure free for more than 12 months (Tables 1 and 2).

AED Treatment Profile

AED monotherapy was received by 100 patients, dual therapy by 69 patients, triple therapy by 24 patients, four AEDs by 4 patients, and five AEDs by 3 patients. There were 21 types of two-drug combinations and 17 types of three-drug combinations. The mean number of AEDs/person was 1.7 ± 0.9, with 30% on old,

Table 2 – Clinical characteristics of seizures among patients on AED monotherapy and polytherapy.

Variables	Monotherapy (n = 100)	Polytherapy (n = 100)	Significance level* (χ^2 test)
Seizure frequency			
1 and above per month	9	14	$P = 0.003$
4–11 per year	4	19	
1–3 per year	51	43	
Absent	36	24	
Percentage of patients who reported ADR	47	75	$P = 0.0001$
Generalized seizures	49	35	$P = 0.062$
Partial seizures	51	65	

AED, antiepileptic drug; ADR, adverse drug reaction.
* $P < 0.05$.

38.5% on new, and 31.5% on combination AED therapy (Tables 2 and 3).

The most frequent new AED monotherapy received was clobazam in 37% and oxcarbazepine in 20% of the patients. The use of clobazam was also maximum (63%) in the polytherapy regimen. A significantly higher number of patients with partial seizures received carbamazepine than did those with generalized seizures (28.4% vs. 10.7%; $P = 0.003$), while the use of sodium valproate and lamotrigine was significantly higher in patients with generalized epilepsy ($P = 0.004$ and 0.048, respectively).

The frequency of seizures and ADRs was significantly higher among patients on polytherapy than among those on monotherapy ($P = 0.0001$ and 0.003 respectively) (Tables 4 and 5) and was strongly associated with a lower QOL score ($P < 0.0001$). The median number of ADRs was 2.6% and involved the central nervous system followed by the gastrointestinal system and skin. There were 12 serious ADRs—hypersensitivity, drug-induced hematological abnormalities, psychotic disturbances and complex memory loss—and warranted drug discontinuation.

QOL in PWE

The overall QOLIE-10 score was 17.4 to 100, with a mean of 74.9 ± 20.6. Most had an optimal (>50) or high QOLIE score (>70), which implied better QOL, while it was less than 50 in 14% of the patients.

Relationship between QOLIE-10 Scores and Clinical Characteristics

There was no significant association between the demographic variables and overall QOLIE-10 scores. Table 4 shows the relationship of clinical and pharmacotherapy variables with the overall QOLIE score. The mean QOLIE 10 score was significantly higher in seizure-free patients than in those with seizures ($P = 0.002$). Analysis of variance showed a significant association between QOL score and duration of time patients were seizure free (not seizure free vs. >2 years vs. <2 years; $P = 0.006$). Post hoc tests showed significantly higher QOLIE-10 scores in patients who were seizure free for more than 2 years than in those who were not seizure free ($P = 0.009$). Seizure frequency and Engel score were significantly associated with QOLIE-10 score ($P < 0.0001$). On post hoc tests, patients with an Engel score of more than 6 had a significantly lower score than did those with an Engel score of 5 to 6 ($P = 0.019$) and less than 5 ($P = 0.0001$). Patients on monotherapy had a significantly higher QOLIE score than did those on polytherapy ($P = 0.012$), with no significant difference between patients on old and new AEDs. A trend toward lower QOLIE-10 score was seen among patients on combination therapy and was statistically insignificant.

A significantly lower QOLIE score was associated with a younger age of onset of seizures ($P = 0.012$), decreased time since last seizure ($P < 0.0001$), an increased number of AEDs ($P = 0.022$), and a higher number of ADRs ($P < 0.0001$).

Significant Predictors of Poor QOL

Multiple linear regression analysis of significant variables in univariate analysis of overall QOLIE-10 score showed adjusted R^2 as 0.496 for the proposed model of study. An increased number of ADRs (standardized β −0.692; $P = 0.0001$), use of two or more AEDs (standardized β −0.107; $P = 0.050$), and higher seizure frequency (standardized β −0.157; $P = .003$) were significant predictors of poor QOL in PWE.

Comparison of AED Treatment between Old, New, and Combined Therapy

Table 5 shows the pattern of the use of old, new, and combination AED therapy. The percentage of patients under each type of AED therapy did not differ significantly with respect to seizure type, their frequency, and freedom. A total of 79.3% of the patients on combination AEDs reported at least one ADR compared with 55.8% on new and 48.3% on old AEDs ($P = 0.008$). No difference was observed in the overall QOLIE-10 scores between the three types of AED therapy. Patients on combination therapy had lower medication effect domain scores than did those on old AEDs ($P = 0.031$).

Table 3 – Pattern and extent of AED use as monotherapy/polytherapy among patients with partial and generalized seizures.

AEDs	No. of patients (N = 200), n (%)	Monotherapy (N = 100), n	Polytherapy (N = 100), n	Partial seizures (N = 116), n (%)	Generalized seizures (N = 84), n (%)	P*
Old AEDs						
Phenytoin†	51 (25.5)	17	34	34 (29.3)	17 (20.2)	0.188
Carbamazepine†	42 (21)	15	27	33 (28.4)	9 (10.7)	0.003
Sodium valproate	28 (14)	12	16	9 (7.8)	19 (22.6)	0.004
Phenobarbitone†	26 (13)	6	20	16 (13.8)	10 (11.9)	0.832
New AEDs						
Clobazam†	74 (37)	11	63	47 (40.5)	27 (32.1)	0.239
Leviteracetam†	46 (23)	12	34	28 (24.1)	18 (21.4)	0.735
Oxcarbamazepine	43 (21.5)	20	23	26 (22.4)	17 (20.2)	0.731
Topiramate†	17 (8.5)	4	13	11 (9.5)	6 (7.1)	0.62
Lamotrigine	6 (3)	3	3	1 (0.9)	5 (6)	0.048
Clonazepam†	5 (2.5)	0	5	4 (3.4)	1 (1.2)	0.401
Zonisamide	2 (1)	0	2	1 (0.9)	1 (1.2)	1
Gabapentin	1 (0.5)	0	1	1 (0.9)	0 (0)	1

AED, antiepileptic drug.

* Chi-square test for difference in utilization of AEDs among patients with partial and generalized seizures ($P < 0.05$ considered significant).

† The proportion of patients on polytherapy was significantly higher than those on monotherapy for these AEDs (χ^2 test; $P < 0.05$).

Table 4 – Univariate analysis showing the relationship between clinical and pharmacotherapy variables and total QOLIE-10 score.

Variables	QOLIE-10 score, mean ± SD	P*
Seizure type		
Partial (n = 116)	73.96 ± 20.63	t = −0.496
Generalized (n = 84)	75.43 ± 20.66	P = 0.621
Seizure freedom		
Yes (n = 60)	81.43 ± 17.63	t = 3.187
No (n = 140)	71.57 ± 21.14	**P = 0.002**
Seizure freedom†		
No (n =140)‡	71.57 ± 21.14	F = 5.262
<2 y (n = 24)	79.4 ± 17.67	P = 0.006
>2 y (n = 36)‡	82.74 ± 17.73	
Engel score†		
<5 (n = 60)§	80.90 ± 18.28	F = 8.365
5–6 (n = 117)§	73.72 ± 20.42	P < 0.0001
>6 (n = 23)§	60.69 ± 21.32	
Family history		
Yes (n = 32)	74.28 ± 19.81	t = −0.090
No (n =168)	74.63 ± 20.81	P = 0.928
Comorbidities		
Yes (n = 52)	71.01 ± 21.40	t = −1.457
No (n = 148)	75.83 ± 20.24	P = 0.147
Time delay in treatment		
Yes (n = 24)	72.64 ± 23.03	t = −0.49
No (n = 176)	74.84 ± 20.31	P = 0.624
Therapy		
Monotherapy (n = 100)	78.22 ± 18.03	t = 2.53
Polytherapy (n = 100)	70.93 ± 22.39	**P = 0.012**
Type of AED		
Old (n = 60)	78.12 ± 17.15	F = 2.561
New (n = 77)	75.42 ± 20.75	P = 0.080
Combined (n = 63)	69.97 ± 22.82	
Adverse drug reactions		
Yes (n = 122)	65.95 ± 20.28	T = −8.669
No (n = 78)	88.06 ± 12.21	**P < 0.0001**
Suicidality		
Yes (n = 9)	37.35 ± 11.96	t = −6.015
No (n = 191)	76.33 ± 19.23	**P < 0.0001**

AED, antiepileptic drug; ANOVA, analysis of variance; QOLIE-10, Quality of Life in Epilepsy Inventory-10.

* Statistical significance based on t test and ANOVA ($P < 0.05$ considered significant for difference in mean scores).

† For seizure freedom and Engel score, Bonferroni post hoc test was used to identify which of the two groups significantly differ among the three; results not shown, presented as text.

‡ Patients with seizure freedom for more than 2 years had a significantly higher score than did patients with no seizure freedom ($P = 0.009$).

§ Patients with an Engel score of more than 6 had a significantly lower score than did patients with both Engel score of 5 to 6 ($P = 0.019$) and less than 5 ($P < 0.0001$).

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 [15]. To address this objective, the present study examined patterns of AED use and identified the demographic, clinical, and pharmacotherapy characteristics and their influence on QOL in PWE.

Demographic and Clinical Profile

The study sample was characterized by younger age patients unlike developed nations where increasing incidence is reported in the older age groups [16]. Although the number of men was higher, this was not statistically significant in contrast to that reported elsewhere [17]. There was a low rate of unemployment in the productive age group (excluding housewives) in our study, which is in contrast to a European study that recorded a higher unemployment rate, which was attributed to the increased frequency of seizures [10]. Many factors may account for this difference, the most important being a greater compulsion among males to earn as they are often the primary source of support to the families.

The type of seizures was predominantly partial as against most Indian studies carried out elsewhere that report the occurrence of primary generalized seizures [4]. In addition, the observed lower incidence of absence seizures in our study as compared to that in developed countries may probably be due to its underdetection [16]. The occurrence of secondary epilepsy among patients with partial seizures may be attributed to the widespread availability of diagnostic technique such as computed tomography/magnetic resonance imaging to identify single ring-enhancing lesions, which is a characteristic of neurocysticercosis and also points to the higher prevalence of taeniasis in developing countries [18].

AED Treatment Profile

The extent of monotherapy versus polytherapy was similar, unlike most other studies in which monotherapy was the preferred regime. Practice of polytherapy is not in line with the recommended principles of epilepsy treatment. It is generally agreed that if seizures persist after titration to the highest tolerated dose of a single AED, the patient is given a trial of two monotherapies followed by combination therapy [19]. Use of polytherapy, however, may be explained by the fact that this study was carried out in a tertiary care center in which patients are often referred for difficult to control seizures. In addition, there is evidence that supports early initiation of polytherapy in severe epilepsies, particularly when the first AED is partially effective and the probability of seizure freedom with monotherapy is low [15].

Conventional AEDs such as phenobarbitone and valproate are in frequent use in many Indian studies. Their use, however, was replaced by higher proportions of newer AEDs such as clobazam, oxcarbazepine, and levetiracetam. The reduced use of older AEDs despite their low cost and once daily dosing, particularly phenobarbitone, may be explained by their high interaction potential and cognitive adverse effect.

The utilization of new AEDs alone and as combination was found to be higher (70%), a trend similar to that seen in European countries [20], but that was for nonepileptic conditions and this was not considered in the present study. A wide variation has been reported to exist in the use of newer AEDs in different regions and hospital settings in India, ranging from 3% in Eastern India to 40% to 50% in central/southern India [21,22]. The findings of our previous study had shown the use of newer AEDs as add on with conventional AED treatment for which they were initially licensed as against their use as monotherapy, seen in 25% of the patients in the present study, indicating a change in prescribing trends [21]. This is in accordance with the updated National Institute for Health and Care Excellence guidelines, which recommend the use of newer AEDs as potential first-line drugs for

Table 5 – Comparison of variables among groups of patients with epilepsy receiving old, new, and combined AED therapy.

Variables	Old AED (n = 60)	New AED (n = 77)	Combination AEDs (n = 63)	P
Seizure freedom (n = 60), n (%)	22 (36.7)	23 (29.9.5)	15 (23.8)	0.132*
Engel score > 6 (n = 21), n (%)	4 (6.7)	7(9.1)	10 (15.9)	0.326*
ADRs Yes (n = 122), n (%)	29 (48.3)	43 (55.8)	50 (79.3)	0.008*
Medication effects score, mean ± SD	2.48 ± 0.79†	2.36 ± 0.86	2.08 ± 0.94†	**0.03**‡
Cognitive functioning score, mean ± SD	21.13 ± 8.03	20.04 ± 8.56	18.24 ± 9.36	0.175‡
QOLIE-10 overall score, mean ± SD	78.12 ± 17.15	75.42 ± 20.75	69.97 ± 22.82	0.080‡

AED, antiepileptic drug; ANOVA, analysis of variance; QOLIE-10, Quality of Life in Epilepsy Inventory-10.
* Chi-square test ($P < 0.05$ considered significant).
† Medication effect score significantly lower with combination therapy than with old AEDs (post hoc Bonferroni test; $P = 0.031$).
‡ Statistical significance based on ANOVA.

focal/generalized seizures [19], demonstrating the influence of evidence-based practices.

The increasing use of clobazam as an adjunctive in dual and triple regimens for both partial and generalized seizures observed in our study may be justified on the basis of the fact that it is a nonsedating benzodiazepine effective in various seizure types and is well tolerated by all age groups. Although, in principle, monotherapy is preferred, literature supports the efficacy of combination AEDs with different or multiple mechanisms of action for improved seizure control, for example, sodium channel blockers with GABAergic drugs—phenobarbitone and clobazam—or with valproate [23]. The use of such combinations is well accepted as rational prescribing. A few patients, however, received two sodium channel blockers, which may increase the possibility of inducing voltage-dependent sodium block with an increased potential to produce neurotoxic adverse effects such as ataxia, dizziness, and diplopia and may need careful attention. The assumption that such an ADR will be induced is because a relatively larger number of patients on polytherapy experienced an ADR. Hence, careful evaluation of rational combinations of AED polytherapy through regular clinical as well as drug-level monitoring, if feasible, to prevent adverse drug-drug interactions may be considered.

The pattern of AED treatment of partial seizures was found to be similar to earlier studies and was as per recommended guidelines [21,24,25], with a higher proportion of patients on levetiracetam. A recently completed double-blind trial by Brodie et al. [26] has shown that levetiracetam meets International League Against Epilepsy class I criteria for noninferiority to carbamazepine in newly diagnosed epilepsy in terms of efficacy and effectiveness. Subsequently, guidelines have been updated (National Institute for Health and Care Excellence) to include levetiracetam as a potential first-line agent in partial seizures and adjunctive in generalized seizures [15,19].

QOL in PWE

QOLIE-10, an abbreviated questionnaire used to study the impact of different variables, in particular, pharmacotherapy characteristics, showed an optimal QOL, with a mean score of 74.58 ± 20.60, which was higher than that reported in a study from Kerala, India [4]. The previous studies have identified female gender, marital status, low education level, and rural residence to be significantly associated with a low QOLIE score [17,27]. In contrast, results of our study did not reveal any association between demographic variables and QOLIE scores. On a positive note, this may probably be because of the decreased stigma, good social support, and increased awareness about epilepsy among patients attending this tertiary care setup.

In the present study, although lower age of onset of seizures was found to be associated with a poor QOL, a finding reported by Sinha et al. [17], the seizure type did not show an association, unlike that reported in two Indian studies [4,28,29]. The clinical significance of this finding is difficult to explain. The increase in seizure frequency as one of the clinical characteristics has been described as the most relevant determinant of poor QOL scores consistently across many studies [17,28], a similar correlation seen in the present study among patients receiving polytherapy. Alternatively, longer seizure-free duration since the last episode is positively correlated with a good QOL.

Patients on AED monotherapy had significantly better QOL, similar to that reported by Thomas et al. [4]; however, there was no difference in the overall QOLIE-10 scores between old and new AEDs. A study by Gilliam [30] demonstrated a similar finding in seizure-free patients. Furthermore, AEDs' adverse effects, with depression as the only parameter in 195 patients with active epilepsy, significantly correlated with poor QOL ($P < 0.0001$). Also, adverse effects from AED use were found to be the most important factor associated with a worse QOL, even among 101 seizure-free patients who were treated with AEDs for epilepsy [31]. The multivariate analysis including significant variables in a stepwise linear regression model in our study identified the increasing number of ADRs to be the most important predictor of poor QOL followed by seizure frequency and number of AEDs.

The analysis of the use of three types of AED therapies—old, new, and combined—showed no difference in seizure frequency. Also, a significantly greater proportion of patients on combination therapy reported ADRs compared with those on old or new AED monotherapy. The score in the medication effect domain (question in this domain based on adverse effects of AED) among those on combination therapy, however, was significantly lower than among those on old AEDs. This could have possibly elicited a positive response from them when we queried them specifically about individual ADRs and led to the lower score in the medication effects domain. Also, the possibility that these patients did not tolerate the old AEDs well because of drug interactions/enzyme induction and hence were administered new AEDs cannot be ruled out.

It is generally assumed that newer AEDs have the same efficacy as older ones but have better tolerability. We observed, however, the absence of a significant difference in adverse effects of AED or QOL scores between old and new AED monotherapy, similar to the results of a study in seizure-free patients in the Standard and New Antiepileptic Drugs trial. This trial provided high external validity on the effectiveness of old and new AEDs in a pragmatic setting. The trial reported lamotrigine to be most effective when compared with carbamazepine and other new AEDs in focal seizures and valproate to be more effective than

topiramate and lamotrigine in generalized and unclassified epilepsies. It is also now known that new AEDs are not completely free of severe adverse effects, particularly the cognitive and psychiatric adverse effects associated with topiramate and levetiracetam, but have similar efficacy as older AEDs in newly diagnosed patients [32].

To our knowledge, this is the first study in India that evaluated the impact of specific pharmacotherapy characteristics on QOL in PWE as well as the tolerability profile of AED therapy in a naturalistic setting. The pattern of AED use did not show a significant difference in use between older and newer AEDs. A few limitations of the present study include the cross-sectional design, which made it difficult to comment with certainty on the differences in efficacy, tolerability, and QOLIE scores between different AED therapies. Ideally, a follow-up study with initiation of AED therapy within the same time frame should enable measurement of difference in QOLIE scores from baseline. Also, patients not conversant with English language had to be explained the various domains in the questionnaire in a local language to elicit responses. Findings, however, revealed increase in seizure frequency, use of polytherapy, and number of ADRs as poor predictors of QOL.

The findings are debatable because there was frequent use of new AEDs, which are generally more expensive, raising the primary concern whether their use should be promoted in developing countries where medication costs are out-of-pocket expenses for patients. In addition, the negative impact of AED polytherapy on QOL and the increased number of adverse reactions emphasize the need to optimize monotherapy regimes. The key to epilepsy management is to adapt treatment decisions to individual patient characteristics where the AED choice is determined by patient-specific features such as age as identified in the present study. The increase in the number of ADRs with a low score in the medication effect domain among patients who received combination therapy hints at the possibility of decreased tolerability to old AEDs. Thus, where enzyme induction and drug interactions are anticipated as significant problems, resulting in reduced tolerability with old AEDs especially in patients with comorbidities, new drugs would be preferable because they play an important role in difficult to control epilepsy encountered in most tertiary care centers.

Conclusions

We conclude that appropriate tools for early detection and selection of safer AED treatment options, with careful monitoring, recognition, and assessment of adverse effects of AEDs, play a crucial role to move us closer to the ultimate goal of freedom from seizures and to achieve optimal QOL in PWE.

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