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Original Article

Pharmacology Section

Comparison of Anti-Epileptic Drugs in Terms of Treatment Outcomes, Adverse Effects and Quality of Life

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ABSTRACT

Introduction: Epilepsy is a disorder of the nervous system requiring prompt medical care and life-long treatment. Unfortunately, data regarding efficacy, Adverse Drug Reactions (ADRs) and Quality Of Life (QOL) in patients using different Anti-Epileptic Drugs (AEDs) is sparse.

Aim: To evaluate five AEDs in comparison for efficacy in reducing seizures, improvement in QOL and ADRs due to the prescribed drug.

Materials and Methods: In this cohort study, 81 epilepsy patients (age >10 years) receiving the following drugs: Levetiracetam, Lacosamide, Oxcarbazepine, Valproate and Phenytoin for atleast six months were enrolled. Quality of Life in Epilepsy Inventory–31 (QOLIE-31) questionnaire was used for measuring the QOL. Efficacy of AEDs was measured on the basis of seizure control, QOL and adverse effects. All the patients were followed-up weekly for six months for treatment response and adverse effects. Overall, QOLIE scores were calculated. T-tests, analysis of variance and regression analysis were used wherever appropriate. The p-value <0.05 was considered statistically significant.

Results: Seizure control was reported in 79% of the patients. A total of 43.2% patients were reported to have experienced an ADR during the course of the study. Adverse events predominantly affected gastroenterologic, psychiatric and general body systems. Patients on Levetiracetam had the best QOL and phenytoin the least.

Conclusion: Better seizure control, high medication adherence and improved QoL was seen in patients with Levetiracetam; followed by Lacosamide, Oxcarbazepine, Valproate and least in Phenytoin.

Keywords: Causality assessment, Focal epilepsy, Generalised tonic clonic epilepsy, Medication adherence, Seizures

INTRODUCTION

Epilepsy remains the major nervous system disorder attacking people from childhood to old age. Approximately, 50 million people worldwide and around 1 crore people in India are epileptic [1,2]. Epilepsy is the pathologic and enduring tendency of the brain to have recurrent seizures [3]. Self-annihilation, fear, stress, depression and accidental death are common among epilepsy patient's [4].

Seizure cessation and prevention of ADRs thus remains the ultimate goal of epilepsy treatment. Optimum therapeutic benefit requires long term commitment and compliance to AEDs [5]. Despite low cost and wide availability of older AEDs, newer AEDs are the preferred choice of epileptologists [6]. In the past decade much research has been focused on either comparing drugs of monotherapy or comparing older anti-epileptics to the newer ones [7,8]. Fewer studies have focussed on the health related QOL of the patient and the ADRs associated with the prescribed medications [7,8]. Further, these studies did not evaluate all the drugs for effect on seizure control and variables that may act as predictors for seizure control.

Thus, present study was designed to evaluate effectiveness of AEDs, predictors of seizure control, ADRs, medication adherence and QOL in epilepsy patients.

MATERIALS AND METHODS

An observational cohort pilot study was performed on generalised tonic clonic and focal epilepsy patients for six months (December 2017-May 2018) in the Neurology Department of Owaisi Hospital and Research Centre, Hyderabad, Telangana, India. Institutional Ethical Review Board acceptance (IRB approval number 2017/19/006) was procured. A sample of 100 was selected in which 81 patients met the inclusion criteria who were receiving any of the five AEDs; Levetiracetam, Phenytoin, Sod. Valproate, Oxcarbazepine, and Lacosamide as Monotherapy for atleast six months.

Selection Criteria and Data Collection

Male and female epilepsy patients, aged 10 years or older receiving AEDs and accepting to participate in the study were included. Patients that were pregnant, patients with a reported head injury, drug induced epileptic seizures, patients with progressive neurological diseases, patients with mental disorders, severe psychological problems, strokes, cerebral tumours, and patients who have had recent brain operation were excluded.

A patient profile sheet specially designed **[Annexure-1]** was used to collect data on therapeutic, socio-demographic and clinical parameters. The medication data collected comprised of generic/brand name, daily dose and safety profile after the administration of the drug.

Measures

Drug monitoring for seizure control: In patients that continued to have seizures, an increased dose was considered up to maximum level as long as no unwanted effects occurred. In patients having adverse effects that are dose-related, a dose reduction was considered. All the patients were followed-up weekly for six months for treatment response and adverse effects.

The ADR profile: The ADR profile includes: [i] type of ADR; [ii] The causality relationship of the ADR with suspected drug according to Naranjo ADR probability scale [9].

Assessment of medication adherence: The Morisky Medication Adherence Scale-4 was used to measure the medication adherence of the patient before and after patient counselling. Patient counselling was done individually by the study investigators. The Morisky Medication adherence scale uses a 5 point scale from 0 to 4 to categorise the patient as non-adherent, moderately adherent and completely adherent [10].

The QOL assessment: The QOLIE-31 questionnaire was used to assess the QOL every four weeks. The QOLIE-31 consists of seven

item scales, consisting of seizure anxiety, emotional satisfaction, energetic/restlessness, memory, treatment effects, community based effects, health status and QOL [11]. The questionnaire translations were delivered to patients in English, Hindi, Urdu and Telugu and the answers were documented in patient information sheet.

STATISTICAL ANALYSIS

Descriptive statistical analysis was carried out using MS excel (2016 version) spread sheet to generate graphs, tables, etc., for the study. All statistical analysis was performed using Epi Info software version 7.0 (CDC., Atlanta, Georgia, USA). Continuous data were presented as mean±SD and categorical data was presented as frequencies and percentages. Continuous variables were compared using student's t-test and analysis of variance (ANOVA). Statistical significance was set at a two sided p-value of < 0.05. Linear regression was used to find the effect of predictor variables on QOLIE t-scores. Logistic regression was used to evaluate the effect of various predictor variables on seizure control. Associations were evaluated by correlation coefficients and odds ratios for linear and logistic regression respectively with 95% confidence intervals.

RESULTS

Baseline Characteristics

A total of 81 patients were medically examined during the study period in the Neurology Department of Owaisi Hospital and Research Centre, Hyderabad and achieved the inclusion criteria within the study duration. Summary of the patient characteristics have been shown in [Table/Fig-1].

The majority were males (54%) and the median age was 44 years. Type of seizure was predominantly generalised with 85% of the patients and 15% with focal epilepsy. Most number of patients (18) was recorded in the age group of 50-59 and the least (3) in the age group of 80-90. Majority of males (10) and females (8) were reported in the age group 50-59. The majority of the population was married and unemployed [Table/Fig-1].

Parameters	Category	N=81; n (%)
Sex	Male	44 (54.3)
	Female	37 (45.6)
Age (years)	Mean age±sd	42.691±19.481
	Median	44
Marital status	Married	60 (74)
	Unmarried	21 (25.9)
Employment status	Employed	26 (32)
	Unemployed	55 (67.9)
Smoking	Smokers	19 (23.4)
	Non-smokers	62 [76.5]
Alcohol	Alcoholic	9 (11.1)
	Non-alcoholic	72 [88.8]

[Table/Fig-1]: Socio-demographic profile of the patients.

Assessment of Medication Adherence

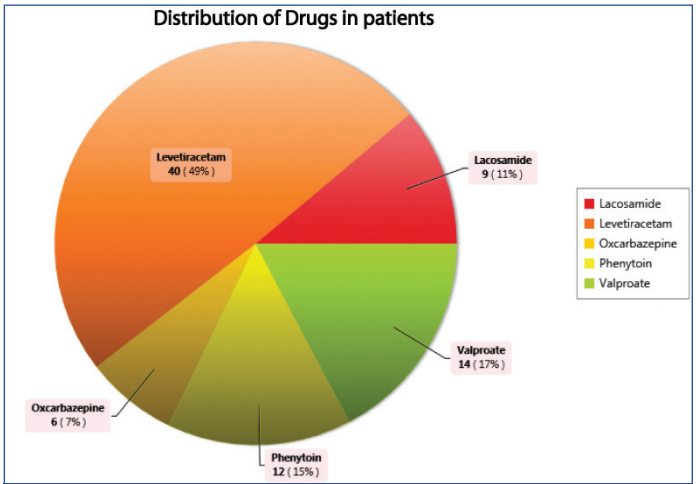
Medication adherence in patients before patient counselling differed significantly after given patient counselling. [Table/Fig-2] shows the difference in the MMAS (Morisky Medication Adherence Score) from the AED before and after three months of patient counselling.

AED Treatment Profile

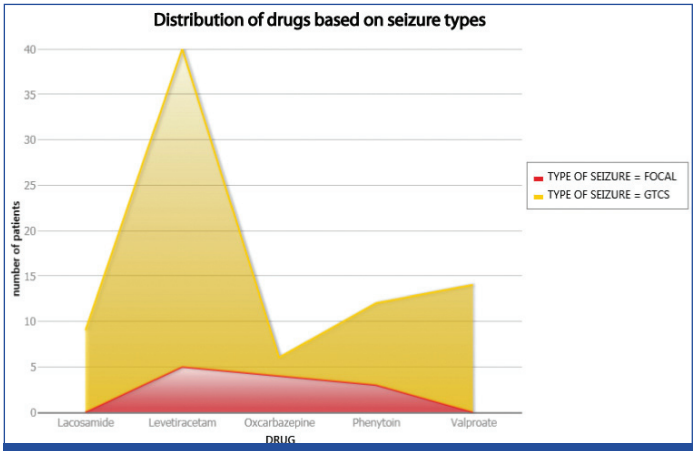
A total of 81 patients received AEDs as monotherapy. The percentage of patients with generalised seizures (69) and focal seizures (12) were found to be 85% and 15%, respectively. The most frequently received AED was Levetiracetam in 49% and least was Oxcarbazepine in 7% of the patients [Table/Fig-3,4].

Drug	MMAS (before)	MMAS (after)	p-value (paired t-test)
Levetiracetam	1.82±0.69	3.56±0.49	p=0.0001
Phenytoin	1.66±0.74	3.50±0.50	p=0.0001
Sod. Valproate	1.98±0.45	3.71±0.45	p=0.0001
Oxcarbazepine	2.33±0.74	3.83±0.37	p=0.002
Lacosamide	2.11±0.73	3.77±0.41	p=0.0005

[Table/Fig-2]: Medication adherence from AED use before and after patient counseling.
Before and after MMA scores were compared using Paired t-test



[Table/Fig-3]: Distribution of drugs in patients.



[Table/Fig-4]: Distribution of drugs based on seizure types.

ADR Profile

Sodium valproate was associated with higher number of ADRs [Table/Fig-5]. Majority of ADRs involved the gastrointestinal system followed by the psychiatry and central nervous system. A serious ADR reported with phenytoin was drug induced hypersensitivity reaction. [Table/Fig-6] indicate the frequently reported ADRs from the AEDs and their causality assessment from the Naranjo Assessment Scaling of Probable, Possible and Definite.

Seizure Control

Seizure Control was 100% with Oxcarbazepine followed by Lacosamide with 89% and Levetiracetam with 80% [Table/Fig-7,8].

QOL Assessment and Seizure Control

From the overall QOL scoring, optimal or high QOLIE score was reported in majority of the patients implying better QOL. Generalised and partial seizures did not differ significantly with respect to QOL score. QOLIE scoring differed significantly between groups of drugs, with high QOL seen in Levetiracetam, while it was least in patients receiving phenytoin [Table/Fig-9]. None of the predictors were able to explain QOL [Table/Fig-10]. In the multivariable model, only age was significantly associated with seizure control [Table/Fig-11].

Adverse effects	AED					Total
	LEVIPIL [AD: 500 mg]	ATOIN [AD: 100 mg]	LACOSET [AD: 100 mg]	OLEPTAL [AD: 150 mg]	NAVALIN [AD: 200 mg]	
Dizziness	-	1	2	-	1	4
Headache	4	-	-	-	-	4
Somnolence	1	-	-	1	-	2
Irritability	4	1	1	-	-	6
Aggression	-	-	1	-	-	1
Rash	-	2	-	-	-	2
Hair loss	-	1 (Focal epilepsy)	-	-	-	1
Nausea	1	-	-	-	7	8
Fatigue	-	-	2	-	-	2
Back pain	-	-	-	2 (Focal epilepsy)	-	2
Fever	-	1	-	-	-	1
Weight gain	-	-	-	-	2	2

[Table/Fig-5]: Distribution of ADRs based on drugs.
LEVIPIL: Levetiracetam; ATOIN: Phenytoin; LACOSET: Lacosamide; OLEPTAL: Oxcarbazepine; NAVALIN: Sodium Valproate; *AD: Average Dose; Only Back pain and Hair loss were ADRs found in Focal epileptic patients; Rest all the ADRs were seen in generalised epilepsy patients

Drug	Frequently reported ADR	Naranjo scale
Levetiracetam	Headache	Probable
	Irritability	Probable
Phenytoin	Rash	Definite
	Hypersensitivity reactions	Probable
Sodium Valproate	Weight gain	Possible
	Nausea	Possible
Oxcarbazepine	Somnolence	Possible
	Back pain	Probable
Lacosamide	Fatigue	Probable
	Dizziness	Possible

[Table/Fig-6]: Frequently reported ADRs.

Drug	Frequency	Percent
Lacosamide	8/9	89%
Levetiracetam	32/40	80%
Oxcarbazepine	6/6	100%
Phenytoin	9/12	75%
Sodium Valproate	9/14	64%
Total	64	100.00%

[Table/Fig-7]: Seizure control based on drug.

a) Sex=Female					
Seizure control	Frequency	Percent	Cum. percent	Exact 95% LCL	Exact 95% UCL
No	5	13.51%	13.51%	4.54%	28.77%
Yes	32	86.49%	100.00%	71.23%	95.46%
Total	37	100.00%	100.00%		
b) Sex=Male					
Seizure control	Frequency	Percent	Cum. percent	Exact 95% LCL	Exact 95% UCL
No	12	27.27%	27.27%	14.96%	42.79%
Yes	32	72.73%	100.00%	57.21%	85.04%
Total	44	100.00%	100.00%		

[Table/Fig-8]: Seizure control based on gender.

DISCUSSION

Epilepsy treatment aims to eliminate seizures, minimise adverse effects and improve QOL of patients. Severe adverse effects and continued seizures are sufficient reasons for discontinuation of an antiepileptic drug. Non-compliance with medication of can be the single most common reason for treatment failure and can be changed by proper patient counselling. The treatment success of an epileptic patient is again dependent on enhancement of QOL and tolerability of antiepileptic drug [7,8]. Thus, inclusion of QOL outcomes in treatment plan along with analysis of seizure frequency and ADRs is therefore the need of the time [10]. To address these objectives, present study compared AEDs in terms of seizure cessation, adverse effects and QOL.

Demographic and Clinical Profile

Older age people were scarce in our study as opposed to advanced nations where increasing occurrence of epilepsy is found in elderly people [12]. The number of men was approximately equal to women which were contrary to that described in other studies [13]. There was a high number of unemployed in our study which was similar to a European study that documented a higher unemployment rate [10]. Majority of the seizures were generalised similar to a study that details the prevalence of primary generalised seizures [14]. Epilepsy studies advocate monotherapy as the first line treatment and polytherapy is only preferred when maximum dose of single antiepileptic drug fails to stop seizures [15,16]. Moreover, as most other studies prefer a monotherapy regimen and comparison to polytherapy will be inconclusive, only patients on monotherapy were included in our study [7,15-17].

AED Treatment Profile

Despite high cost, newer antiepileptics have now replaced older AEDs like Phenytoin and Sodium Valproate. The reduced use of older AEDs describes their lower tolerability and significant harmful profile [18]. These results have been replicated by our study which shows that Levetiracetam, Oxcarbazepine and Lacosamide show better seizure control than Phenytoin and Valproate. The increasing use of Levetiracetam observed in present study may be rationalised on the fact that it is useful in various seizure types and is having good safety profile in all age groups. It's a common assumption that efficacy of newer and older AEDs is similar but safety profile is better with newer AEDs [10,19,20]. While literature search returned many studies, these are limited to one drug versus placebo as monotherapy or between two AEDs which does not allow us to make direct comparison of all AEDs at one time. Moreover, other studies [Table/Fig-12] show Valproate being better than Levetiracetam, Phenytoin and Oxcarbazepine in many cases as opposed to the present study where levetiracetam was found to be better than valproate [17,21-25].

Quality of Life and Seizure Control

The influence of various factors on QOL was measured using the QOLIE-31 questionnaire. Earlier studies have proved female sex, matrimonial status; high illiteracy and agrarian habitation to be significantly related with a decreased QOL [12,26]. Our results depicted significant association between presence of ADR and low QOLIE scores but was not found to be statistically significant.

a) QOLIE T score											
QOLIE T score * drug	Obs	Total	Mean	Var	Std Dev	Min	25%	Median	75%	Max	Mode
Lacosamide	9	529	58.7778	19.4444	4.4096	52	55	60	62	65	55
Levetiracetam	40	2381	59.525	65.3327	8.0829	42	54.5	61.5	66	71	66
Oxcarbazepine	6	319	53.1667	54.5667	7.3869	47	47	50	62	63	47
Phenytoin	12	615	51.25	124.5682	11.161	36	38.5	55.5	61	65	36
Valproate	14	730	52.1429	56.1319	7.4921	40	46	50	60	63	45
b) ANOVA, a Parametric test for inequality of population means.											
Variation	SS	df	MS	F statistic							
Between	1075.8447	4	268.9612	4.0267							
Within	5076.3282	76	66.7938								
Total	6152.1728	80									
p-value	0.0051										

[Table/Fig-9]: QOLIE T scores based on drug.
*drug name

Variable	Coefficient	95% Confidence	Limits	Std error	F-test	p-value
ADR	-3.878	-8.102	0.346	2.12	3.3463	0.071386
Age	0.002	-0.101	0.105	0.052	0.0015	0.968732
Alcoholic	-1.511	-8.494	5.472	3.505	0.1858	0.667665
Sex	-2.457	-7.289	2.374	2.425	1.0269	0.31419
Smoker	1.06	-4.297	6.417	2.688	0.1554	0.694536
Type of seizure	2.626	-2.977	8.229	2.812	0.8719	0.353467
Constant	58.711	52.845	64.577	2.944	397.7222	0

[Table/Fig-10]: Predictors of QOLIE t score.
Correlation coefficient: r^2=0.10

Term	Odds ratio	95%	C.I.	Coefficient	S.E.	Z-statistic	p-value
ADR (Yes/No)	0.3409	0.0918	1.2657	-1.0762	0.6693	-1.6079	0.1079
Age	0.9528	0.9195	0.9873	-0.0484	0.0181	-2.6655	0.0077
Alcoholic (Yes/No)	0.4346	0.0739	2.5546	-0.8334	0.9037	-0.9222	0.3564
Sex	2.4887	0.5968	10.3779	0.9117	0.7286	1.2515	0.2108
Type of seizure (Yes/No)	1.2718	0.1968	8.2207	0.2404	0.9522	0.2525	0.8006
Constant	*	*	*	3.8531	1.0608	3.6321	0.0003
Convergence:	Converged						
Iterations:	4						
Final-2*Log-likelihood:	66.5851						
Cases included:	81						
Test	**Statistic**	**D.F.**	**p-value**				
Score	16.6653	5	0.0052				
Likelihood ratio	16.6493	5	0.0052				

[Table/Fig-11]: Predictors of seizure control.

Reference	Population/design	Duration	Type of seizure	Outcome	
				Seizure freedom (%) 2	Therapetic inefficacy (%)1
Trinka E et al., [21]	Adults/ unblinded, randomised, superiority trial	12 months	All types	Valproate: 45.5; levetiracetam: 39.5	Valproate: 3.4; levetiracetam: 2.6
Zhu F et al., [22]	Adults/retrospective observational study	7 years	Focal epilepsy	Valproate: 36.90; levetiracetam: 40.10; oxcarbazepine:17.20	Not specified
Chung S et al., [17]	Adults/retrospective observational study	2 years	Focal and generalised epilepsy	Not assessed	levetiracetam: 46.4; Oxcarbazepine: 41.2
Ramsey RE et al., [23]	Adults, children/parallel, randomised, open label, multicenter trial	6 months	Generalised tonic clonic seizures	Valproate:64; phenytoin:53	Valproate:1.1; phenytoin:2
Thilothammal N et al., [24]	Children/Randomised, double blind clinical trial	2 years	Generalised tonic clonic seizures	Valproate:73.7; phenytoin:69.5	Not assessed
Callaghan N et al., [25]	Adults, children/Randomised, double blind clinical study	2 years	Focal and generalised epilepsy	valproate: 59.4; phenytoin: 73.0	Not assessed
Present study Syed AA et al., 2018	10 years or older, male and female, cohort, observational study	6 months	Focal and generalised epilepsy	Oxcarbazepine:100; Lacosamide:89; Levetiracetam:80; Phenytoin:75; Valproate:64	Not assessed

[Table/Fig-12]: Characteristics of the included studies [17,21-25].
Therapeutic inefficacy refers to lack of effect and/or worsening of cases resulting into patient withdrawal from the study. 2-Seizure freedom refers to percentage of people without seizure at the end of the study

Conversely, seizure control, seizure type, age, gender, alcohol intake were not associated with QOLIE scores and seizure control which was in contrast to a study showing seizure type, age and gender as significant predictors of QOL [27]. Results of this study showed that patients on Levetiracetam had the best QOL and phenytoin the least. On the other hand, there are no studies evaluating the predictors of seizure control. In this study, age was found to be significant predictor of seizure control in a multivariable logistic regression model.

Adverse Reactions to Antiepileptic Drugs

ADRs have been one of the important cause of drug discontinuation leading to therapeutic inefficacy [17,21,23]. Conversely, ADRs were not responsible for drug discontinuation in this study which may be due to mild nature of the ADRs. Sodium valproate was the drug having maximum number of ADRs followed by Levetiracetam, Phenytoin, Lacosamide and Oxcarbazepine. Levetiracetam was responsible for headache and irritability which was confirmed by another study. Similarly, rashes and hypersensitivity reactions with phenytoin seen in this study were also reported by other study [28].

LIMITATION

The present study has many limitations. Because the study was designed as a pilot study, sample size and duration of study was small. Only five drugs and two types of epilepsy patients were considered. The influence of comorbid conditions and duration of treatment was not considered while evaluating QOL. As majority of the patients were outpatients, verbal assessment of MMA scores was used to assess medication adherence. Only patients on monotherapy were included whereas polytherapy patients were completely excluded. Ideally the study would have been designed to detect the improvement in QOLIE scores from baseline, which was not possible due to short duration of the study.

CONCLUSION

In conclusion, levetiracetam had better efficacy and tolerability when compared to the other four drugs; and the lowest QOL was seen in patients on phenytoin. The results of the present study advocate that Levetiracetam is the first, Oxcarbazepine and Lacosamide, better and Sodium Valproate and Phenytoin are the last option as monotherapy in epileptic patients. Thus, effective seizure termination and improved QOL can be attained by striking a balance between the efficacy and harmful adverse effects of the drugs.

REFERENCES

[1] World Health Organization. Epilepsy; 2018 [cited 2018 13 July]. Available: http://www.who.int/news-room/fact-sheets/detail/epilepsy.
[2] Santhosh NS, Sinha S, Satishchandra P. Epilepsy: Indian perspective. Ann Indian Acad Neurol. 2014;17 Suppl 1:S3-S11.
[3] Fisher RS, Acevedo C, Arzimanoglou A, Bogacz A, Cross JH, Elger JH, et al. ILAE official report: A practical clinical definition of epilepsy. Epilepsia. 2014;55(4):475-82.
[4] Jones RM, Butler JA, Thomas VA, Peveler RC, Prevett M. Adherence to treatment in patients with epilepsy: Associations with seizure control and illness beliefs. Seizure-Eur J Epilep. 2006;15:504-08.
[5] Kyngas H. Predictors of good compliance in adolescents with epilepsy. Seizure. 2001;10:549-53.
[6] Semah F, Picot MC, Derambure P, Dupont S, Vercueil L, Chassagnon S, et al. The choice of antiepileptic drugs in newly diagnosed epilepsy: A national French survey. Epileptic Disord. 2004;6:255-65.
[7] Marson AG, Al-Kharusi AM, Alwaidh M, Appleton R, Baker GA, Chadwick DW, et al. The SANAD study of effectiveness of valproate, lamotrigine, or topiramate for generalized and unclassifiable epilepsy: An unblinded randomized controlled trial. Lancet. 2007;369:1016-26.
[8] George J, Kulkarni C, Sarma GRK. Antiepileptic drugs and quality of life in patients with epilepsy: A tertiary care hospital-based study. Value Health Reg Issues. 2015;6:1-6.
[9] Naranjo CA, Busto U, Sellars EM, Sandor P, Ruiz I, Roberts EA, et al. A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther. 1981;30:239-45.
[10] Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of self-reported measure of medication adherence. Med Care. 1986;24:67-74.
[11] Cramer JA, Perrine K, Devinsky O, Bryant-Comstock L, Meador K, Hermann B. Development and cross-cultural translations of a 31-item quality of life in epilepsy inventory. Epilepsia. 1998;39(1):81-88.
[12] Perucca E, Tomson T. The pharmacological treatment of epilepsy in adults. Lancet Neurol. 2011;10:446-56.
[13] Ray BK, Bhattacharya S, Kundu TN, Saha SP, Das SK. Epidemiology of epilepsy-Indian Perspective. J Ind Med Assoc. 2002;100:322-26.
[14] Abhik S, Debasish S, Sarmila M, Prasenjit S, Samir D. Factors associated with quality of life of patients with epilepsy attending a tertiary care hospital in Kolkata, India. Neurol Asia. 2011;16:33-37.
[15] Thomas SV, Koshy S, Nair CR, Sarma SP. Frequent seizures and polytherapy can impair quality of life in persons with epilepsy. Neurol India. 2005;53:46-50.
[16] Zeng QY, Fan TT, Zhu P, He RQ, Bao YX, Zheng RY, et al. Comparative long-term effectiveness of a monotherapy with five antiepileptic drugs for focal epilepsy in adult patients: A prospective cohort study. PLOS ONE. 2015;10:e0131566.
[17] Chung S, Wang N, Hank N. Comparative retention rates and long-term tolerability of new antiepileptic drugs. Seizure. 2007;16:296-304.
[18] St Louis EK, Gidal BE, Henry TR, Kaydanova Y, Krumholz A, McCabe PH, et al. Conversions between monotherapies in epilepsy: Expert consensus. Epilepsy Behav. 2007;11:222-34.
[19] Richard H. Mattson-efficacy and adverse effects of established and new antiepileptic drugs. Epilepsia. 1995;36 Suppl 2:S13-26.
[20] Epilepsies: The Diagnosis and Management, London, UK. Clinical Guideline 137. National Institute for Health and Care Excellence (NICE) 2012.
[21] Trinka E, Marson AG, Van Paesschen W, Kälviäinen R, Marovac J, Duncan B, et al. KOMET: an unblinded, randomised, two parallel-group, stratifed trial comparing the effectiveness of levetiracetam with controlled-release carbamazepine and extended-release sodium valproate as monotherapy in patients with newly diagnosed epilepsy. J Neurol Neurosurg Psychiatry. 2013;84(10):1138-47.
[22] Zhu F, Lang SY, Wang XQ, Shi XB, Ma YF, Zhang X, et al. Long-term effectiveness of antiepileptic drug monotherapy in partial epileptic patients: A 7-year study in an epilepsy center in China. Chin Med J (Engl). 2015;128(22):3015-22.
[23] Ramsay RE, Wilder BJ, Murphy JV, Holmes GL, Uthman B, Slater J, et al. Efficacy and safety of valproic acid versus phenytoin as sole therapy for newly diagnosed primary generalized tonic-clonic seizures. Journal of Epilepsy. 1992;5 (1):55-60.
[24] Thilothammal N, Banu K, Ratnam RS. Comparison of phenobarbitone, phenytoin with sodium valproate: Randomized, double blind study. Indian Pediatr. 1996;33(7):549-55.
[25] Callaghan N, Kenny RA, O'Neill B, Crowley M, Goggin T. A prospective study between carbamazepine, phenytoin and sodium valproate as monotherapy in previously untreated and recently diagnosed patients with epilepsy. J Neurol Neurosurg Psychiatry. 1985;48(7):639-44.
[26] Brodie MJ, Perucca E, Ryvlin P, Ben-Menachem E, Meencke HJ. Levetiracetam monotherapy study group-comparison of levetiracetam and controlled-release carbamazepine in newly diagnosed epilepsy. Neurology. 2007;68:402-08.
[27] Shetty PH, Naik RK, Saroja A. Quality of life in patients with epilepsy in India. J Neurosci Rural Pract. 2011;2:33-38.
[28] Cramer JA, De Rue K, Devinsky O, Edrich P, Michael R. Trimble MR. A systematic review of the behavioral effects of levetiracetam in adults with epilepsy, cognitive disorders, or an anxiety disorder in clinical trials. Epilepsy Behav. 2003;4:124-32.

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Annexure 1- Patient data collection form Owaisi Hospital and research center neurology department.

Patient Name:		**IP No.:**	
Sex:		**Age:**	
Height:		**Weight:**	
Educational details:		**Occupation:**	
Address:		**Phone No.:**	
Temp: ^{o}F	**BP:** mmHg	**Pulse:** b/min	**RR:** /min
Present Complaints			
Past Medical History			
Personal History			
Alcoholic: ☐ YES ☐ NO (If chronic please mention);		**Smoker:** ☐ YES ☐ NO	
Others:			
Seizure History			
Time of first seizure:			
Age at first seizure:			
Type of Seizure:			
Seizure duration:			
Seizures within the past one year:		**<20**	**>20**
Family Seizure History			
Family history of epilepsy: ☐ Present ☐ Absent ☐ Unknown (If present, list family member and type);			
Known Genetic syndrome: ☐ Present ☐ Absent ☐ Unknown			
Known mutations in DNA: ☐ Present ☐ Absent ☐ Unknown			
Obstetric History			
Pregnancy: (mention trimester)		**Lactation:**	
Associated Conditions			
☐ None ☐ Known Cerebral palsy ☐ Mental retardation ☐ Autism ☐Dementia			
☐ Neurodegenerative disorder ☐ Ataxia ☐ Migraines☐ Developmental delay ☐ Other (specify);			

Seizure Information

- **Begin Time:** ☐am ☐pm
- **Seizure Duration:** Min Sec

Description Of Seizure:

☐ Biting of tongue/lips ☐ Chewing/ Lip smacking ☐ Crying out ☐Eyes downward

☐ Drooling ☐ Falling to the floor ☐ Eyes upward ☐ Fidgeting with objects ☐ Head and eyes turned to the left ☐ Head and eyes turned to the right ☐ Head Drop

☐ Jerking while conscious ☐ Jerky arm movements left side ☐ Jerky arm movements right side ☐ Loss of bladder control ☐ Loss of bowel control ☐ Nausea/Vomiting

☐ Picking at clothes/ taking off clothes ☐ Rapid blinking of eyes ☐ Rigid body ☐Sudden dropping of objects ☐ Unconscious ☐ Unresponsive ☐ Violent shaking of entire body

☐ Other

- **If Other specify:**

Respiration: ☐Absent ☐Deep ☐ Fast ☐ Normal ☐Shallow ☐ Slow

Skin Colour: ☐ Ashen ☐ Cyanotic ☐Flushed ☐Pale ☐ Pink

Behaviour after Seizure: ☐Complaints of headache ☐Confused ☐Deep Sleep

☐ Dizziness ☐ Drowsiness ☐ Fever ☐ Inability to walk or stand ☐ Irritability

☐ Problems with vision ☐ Return to activity engaged in prior to seizure

- **If Other specify:**

Precipitating factors:

Resulting injuries:

Laboratory Investigations

EEG: ☐ Normal ☐ Epileptiform Abnormalities ☐ Non-Epileptiform Abnormalities

☐ Both Abnormalities ☐ Not Done

- **Generalised spike and wave:** ☐ <2.5Hz slow ☐ 2.5-3.5 Hz ☐ m>3.5Hz
- **Focal spikes:** ☐ Temporal ☐ Extra temporal ☐Multifocal

IMAGING: ☐ MRI ☐ CT ☐None

☐ Normal ☐ Abnormal ☐ Unknown ☐Other (specify)

Other Laboratory Investigations