A Prospective Study to Measure Drug Compliance in Epilepsy Patients

Padala Kalyani*, **Merugu Shravan Goud**

Pharm. D Intern, Department of Pharmacy Practice, Bhaskar Pharmacy College, Yenkapally, Moinabad, Telangana, INDIA.

ABSTRACT

Background: Epilepsy may promote limitations and restrain activities, interfering with the occupational ability, professional goals and social integration of patients. It increases morbidity and symptomatic epilepsy reduces life expectancy by 18 years at maximum. It continues to be a highly stigmatized and disabling chronic condition requiring a lifelong process of adherence to the prescriber's instructions and drug regimens. But many people cannot follow the order and seizure can occur from anti-epileptic drug withdrawal. So, measuring and monitoring of drug compliance is essential. **Method:** Totally 75 epilepsy patients were assessed, among which 60 patients who met the inclusion criteria were recruited into the study and were interviewed by using a structured questionnaire. The survey approach was used in the study. The study period was 6 months. **Results:** Majority (63%) of the sample were compliant to the medication. According to the study, 27% of the sample stated cost factor as the reason for non-compliance. Among 29 (48%) patients who experienced side effects, majority (43%) suffered from drowsiness. Among 21 patients who had history of non-compliance [P-value 0.95 > 0.05 level of confidence], 90% were non-compliant in the present study. Patient counselling was done, and patients were reassessed. **Conclusion:** After reassessment, majority (92%) denied stopping medication in case of 2-3 months continuous absence of seizure episodes. This approach helped in 29% increment in drug compliance status among non-compliant individuals.

Key words: Epilepsy, Structured questionnaire, Measure, Drug-compliance, Patient counselling.

INTRODUCTION

An epileptic seizure is a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain.[1] Epilepsy is a neurological disorder with reported prevalence of 6-8/100,000 incidence of 30-50/100,000 per year and cumulative incidence of 3%. Compliance with medication is a major problem because of the need for long-term therapy together with unwanted effects of many drugs.[2] According to the University of Tennessee Medical Center, there are four common types include Tonic-clonic seizures, Absence seizures, Simple partial seizures, Complex partial seizures.[3] Compliance behavior depends on the specific clinical situation, nature of illness, and the treatment program. An increased complexity of treatment regimen, as well as increased number of required behavioral changes appears to be associated with non-compliance.[4] Patients can accidentally fail to adhere through forgetfulness, misunderstanding, or uncertainty about clinician's recommendations, or intentionally due to their own expectations of treatment, side-effects, and lifestyle choice.[5]

The aim of drug is to control and totally prevent all seizure activity at an acceptable level of side effects.[6] Antiepileptic drugs are selected first and foremost according to clinical efficacy, then tolerability, drug interaction profile, and ease of use.[7] Treatment with standard anticonvulsants is often complicated by side effects. Up to 61 percent of patients with seizures report having side effects with antiepileptic drugs.[8]

AEDs can be narrow or broad spectrum. The narrow spectrum AEDs mostly work

for specific types of seizures (such as partial, focal, or absence, myoclonic seizures). Broad spectrum AEDs additionally has some effectiveness for a wide variety of seizures (partial plus absence myoclonic seizures).[9] Poor adherence to medication is major problem to sustained remission and functional restoration resulted in treatment failure and seizure recurrence.[10]

Medication adherence should be discussed regularly with the patient, and when a treatment seems to fail. There are several types of non-adherence. Therapeutic or medication non-adherence which includes failure to have the prescription dispensed or renewed, omission of doses, errors of dosage, incorrect administration, errors in the time and frequency of administration, and premature discontinuation of the drug regimen. A second type of non-adherence is dietary/exercise non-adherence in which the patient fails to follow the diet and exercise recommendations. A third type is the appointment non-adherence at which the patient fails to show up at clinics for the scheduled checkup.[11] AEDs non-adherence will also lead to increase burden of inpatient and emergency department services; moreover, it also affects the family members socially, economically, and psychologically.[12]

OBJECTIVES

The main objectives of the study were to measure the drug compliance among epilepsy patients attending the Tertiary care hospital. The significance of the study is to find the major factors that are responsible for the noncompliance in the selected population there by counseling the patients and creating the awareness about the importance of the drug compliance and its positive effects on their quality of life, better seizure control and decreasing the hospitalization, morbidity and mortality.

METHODS AND METHODOLOGY

- **Plan of work** Study to measure drug compliance, preparation and submission of protocol, questionnaire, informed consent document to the hospital. Thereby obtaining Ethical Committee approval. The data was collected from the patients attending hospital; patients were interviewed by using a structured questionnaire. A survey method is used in this study. Drug compliance level was measured and there by identifying the factors affecting drug compliance. Awareness among patients is created by patient counseling. Reassessment about the drug compliance levels was done. The results were obtained by descriptive statistics.

- **Study site** the research study was conducted in Tertiary care hospital.

- **Study design** It is a prospective observational study and uses self-prepared questionnaire.

- **Description of the tool** Structured questionnaire or data collection form contains three parts, in which Part-I contains demographic details, Part-II contains disease data and Part-III contains medication data.

- **Study period** the study was conducted for six months.

- **Inclusion criteria** Patients with age above 12 years, Patients with epilepsy and other co-morbid diseases.

- **Exclusion criteria** Patients not providing ICD, Pediatric population was excluded, patients not willing to answer.

- **Sources of data** Case reports, laboratory data, interviewing patients, patients' care giver and physician.

- **Sample** people with epilepsy.

- **Sample size** 60 patients.

- **Sampling technique** purposive sampling.

- **Pilot study** A small study was conducted in advance of a planned project, specifically to test aspects of the study design and to allow necessary adjustment before final commitment to the design.[13]

- **Plan of analysis** A plan of analysis was developed after a pilot study. The data collected was coded, entered in the excel sheet and analyzed by descriptive statistics using chi-square test.

- **Ethical committee approval** Protocol of the study was submitted to hospital ethical committee. After the agreement by the hospital ethical committee members, it was approved by the ethical committee of Chakrapani Neuro Care Hospital, Nizamabad, Telangana.

RESULTS

Sample according to sex: Majority of patients suffering from seizure disorder are male patients. Among 60 (100%) patients, there were 39 (65%) male patients and 21 (35%) female patients.

Marital status: Majority of patients suffering from seizure disorder are married. Among 60 (100%) patients, 31 (52%) patients are married and 29 (48%) patients are unmarried.

Residence: Majority of patients belonged to rural area. Among 60 (100%) patients, there were 58 (97%) patients from rural area 2 (3%) patients from urban area.

Educational status: Majority of sample had school education. Among 60 (100%) patients, 28 (47%) patients have school education, 20 (33%) patients have no educational qualification, 4 (7%) patients are graduates and 2 (3%) patients are post graduates.

Employment status: Majority of the patients are employed. Among 60 (100%) patients, 34 (57%) patients are employed and 26 (43%) patients are unemployed.

Type of family: Majority of the sample belongs to nuclear family. Among 60 (100%) patients, 52 (87%) patients belong to nuclear family and 8 (13%) patients belong to joint family.

Family history of epilepsy: Majority of sample does not have family history of epilepsy. Among 60 (100%) patients, 46 (77%) patients do not have family history of epilepsy and 14 (23%) patients have family history of epilepsy.

Age of onset of epilepsy: Majority of patient's age of onset of epilepsy was above 18 years. Among 60 (100%) patients, 23 (39%) patients' age of onset of epilepsy was in between 5 to 18 years and only 8 (13%) patients' age of onset of epilepsy was below 5 years.

Years of illness: Majority of the patients have been suffering from epilepsy from past 1 year to 10 years. Among 60 (100%) patients, 32 (53%) patients have been suffering from epilepsy from past 1 year to 10 years, 15 (25%) patients have been suffering from epilepsy since a few months, which is less than a year.

Type of therapy: Majority of the sample follows polytherapy. Among 60 (100%) patients, 41 (68%) patients are following polytherapy and 19 (32%) patients are following monotherapy. The most commonly prescribed combination is Phenytoin and Valproic acid.

Frequency of medication: Majority of the patients were administering AEDs two times a day. Among 60 (100%) patients, 52 (87%) patients were receiving AEDs twice a day, 6 (10%) patients were receiving AEDs thrice a day and only 2 (3%) patients were receiving AEDs once a day.

Reason for drug noncompliance: Out of 22 (100%) patients who were non-compliant, majority stated uncategorized reasons i.e., 9 (41%) patients had uncategorized reasons, 6 (27%) patients stated cost factor as the reason for noncompliance, 4 (18%) patients often forget to take medication, 3(14%) patients stated that they did not benefit.

Previous history of noncompliance: Majority of the sample did not have previous history of noncompliance. Among 60 (100%) patients, 39 (65%) patients did not have any previous history of noncompliance, whereas 21 (35%) patients have previous history of noncompliance.

Family members reminding to take medicine: Majority of the sample was not reminded to take their medication by family members. Among 60 (100%) patients, 38 (63%) patients do not need anybody's assistance and 22 (37%) patients need to be reminded about the medication.

Development of side effects Majority of the sample did not experience any side effects i.e., among 60 (100%) patients, 31 (52%) patients did not experience any side effects whereas, 29 (48%) patients experienced side effects.

Side effects effecting work: side effects were not problematic for majority of the patients. Among 60 (100%) patients, 44 (73%) patients are not affected by the side effects, whereas 16 (27%) patients were affected by the side effects that are developed due to AED therapy.

Easy availability of medicine: Majority of patients had easy availability of medicines. Among 60 (100%) patients, 58 (97%) patients had easy availability of medicines and only 2 (3%) patients had problem with availability of medicines.

Monthly Medicine Expenditures in Rupees: majority of the patients had monthly expenses up to Rs.1000/. Among 60 (100%) patients, 42 (70%) patients had monthly expenses of about Rs.1000/-, 16 (27%) patients had monthly expenses in between Rs.1001/- to Rs.2000/- and only 2 (3%) patients had monthly expenses more than Rs.2000/-.

Follow up regularity: Majority of the patients who attended follow ups regularly. Among 60 (100%) patients, 59 (98%) patients attended regular follow ups and only 1 patient was irregular.

Table 1: Distribution of sample by diagnosis.

Diagnosis	Frequency	Percentage
CPS	22	36
Febrile seizures	1	2
GTCS	28	47
Refractory seizures	2	3
Simple partial motor seizure	1	2
Status Epilepticus	6	10
Grand Total	60	100

- Among 60 patients, there were 28 (47%) patients with GTCS, 22 (36%) patients with CPS, 6 (10%) patients with SE, 2 (3%) patients with Refractory seizures, 1 (2%) patient with Febrile seizures, and 1 (2%) patient with Simple partial motor seizures.

Table 2: Distribution of sample according to age.

Age Category	Frequency	Percentage
12 – 20	22	37
21 – 40	24	40
40 – 50	8	13
> 50	6	10
Total		

- The age of the patients in the selected sample ranged from 12 – 62. Mean is the average age of the patients suffering from seizure disorder is 29.2. Median is the central tendency of the age of the patients who are suffering from seizure disorder is around 25. Mode is the patients who are suffering from seizure disorder are mostly at the age of 15.

Table 3: Distribution of sample according to usage of drugs.

Name of AED	Frequency	Percentage
Phenytoin	30	32
Valproic acid	32	34
Levetiracetam	10	11
Oxcarbamazepine	10	11
Clobazam	7	7
Carbamazepine	4	4
Phenobarbitone	2	2
Total	95	100

- Majority of the patients were using Valproic acid [34%] and Phenytoin [32%].
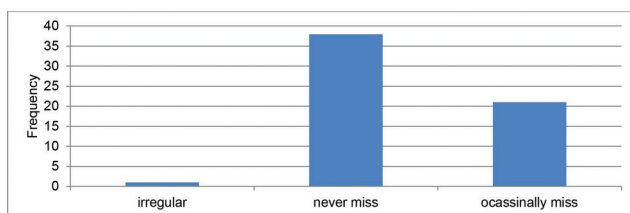

Figure 1: Distribution of sample according to compliance to AEDs.

- Majority of the sample are compliant to the medication. Among 60 (100%) patients, 38 (63%) patients never missed their dose and are compliant to the AEDs, 21 (35%) patients occasionally missed their dose and 1 (2%) patient was taking medicines irregularly.
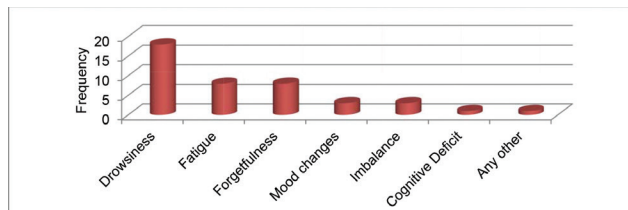

Figure 2: Distribution of Sample According to Type of Side Effects.

- Majority of sample experienced drowsiness [43%], and then followed by fatigue [19%], forgetfulness [19%], mood changes [7%], and imbalance [7%].
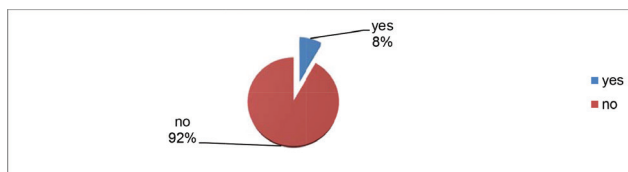

Figure 3: Distribution of Sample according to Patients Willing to Stop the medication if No Seizure Episode.

- Majority of patients denied stopping medication in case of 2-3 months continuous absence of seizure episodes. 5 (8%) patients were willing to stop medication in case of 2-3 months continuous absence of seizure episodes.

- The objective of measuring the drug compliance in the epilepsy patients was attained and found to be 63%.

Factors influencing drug compliance

Failure to comply with drug regimens is prevalent amongst patients with epilepsy and the consequence of this is often an increased risk of further seizures.[14] Interpretation of data enables to check the dependency of each factor. The evaluation further gives information about the factors that contribute to the drug noncompliance.

DISCUSSION

For individuals with epilepsy, adherence to medication is crucial in preventing or minimizing seizures and their cumulative impact on everyday life. Non-adherence to antiepileptic drugs (AEDs) can result in breakthrough seizures many months or years after a previous episode and can have serious repercussions on an individual's perceived quality of life.[15]

Table 4: Factors influencing drug compliance

Variables	Category	Compliant frequency	Non-complaint frequency	Total	Chi square test	P-value
Age	<29	21	12	33	0.957	0.25
	>29	17	10	27		
		38	**22**	**60**		
Education	School	18	10	28	0.224	0.5
	>School	20	12	32		
		38	**22**	**60**		
Place	Urban	1	1	2	0.274	0.5
	Rural	37	21	58		
		38	**22**	**60**		
Duration of Illness	<10	30	17	47	0.423	0.5
	>10	8	5	13		
		38	**22**	**60**		
History of non-Compliance	Present	13	8	21	0.000	0.95
	Absent	25	14	39		
		38	**22**	**60**		
Side effects	Present	18	11	29	0.464	0.25
	Absent	20	11	31		
		38	**22**	**60**		
Expenditure of medicine	<500	12	7	19	0.257	0.5
	>500	26	15	41		
		38	**22**	**60**		

Variables	Category	Compliant frequency	Non Compliant frequency	Total	chi square test	p-value
Sex	Female	12	9	21	0.465	0.25
	Male	26	13	39		
		38	**22**	**60**		
marital status	Married	19	12	31	0.734	0.25
	Unmarried	19	10	29		
		38	**22**	**60**		
employment status	Employed	19	15	34	0.171	0.5
	Unemployed	19	7	26		
		38	**22**	**60**		
type of family	Joint	4	4	8	0.401	0.5
	Nuclear	34	18	52		
		38	**22**	**60**		
family h/o epilepsy	No	30	16	46	0.583	0.25
	Yes	8	6	14		
		38	**22**	**60**		

age at which you were diagnosed to have epilepsy	0-5yrs	6	2	8	0.431	0.5
	5-18yrs	16	7	23		
	>18yrs	16	13	29		
		38	**22**	**60**		
type of therapy	Monotherapy	15	4	19	0.088	0.75
	Polytherapy	23	18	41		
		38	**22**	**60**		
	OD	1	1	2	0.702	0.25
how frequently do you take medicine	BID	34	18	52		
	TID	3	3	6		
		38	**22**	**60**		
family member reminding to take medicine	No	25	13	38	0.604	0.25
	Yes	13	9	22		
		38	**22**	**60**		
side effects affecting work	No	27	17	44	0.600	0.25
	Yes	11	5	16		
		38	**22**	**60**		

Table 5: Percentage table of factors influencing drug compliance

Variables	Category	Compliant frequency (%)	Non-compliant frequency (%)	Total
	<29	64	36	100
Age	>29	63	37	100
	School	71	29	100
Education	>School	56	44	100
	Urban	100	0	100
Place	Rural	62	38	100
	<10	66	34	100
Duration of Illness	>10	54	46	100
	Present	10	90	100
History of non-Compliance	Absent	92	8	100
	Present	59	41	100
Side effects	Absent	68	32	100
	<500	74	26	100
Expenditure of medicine	>500	59	41	100

Variables	Category	compliant frequency %	non-compliant frequency %	total%
	Female	57	43	100
Sex	Male	67	33	100
	Married	61	39	100
Marital status	Unmarried	66	34	100

Employment status	Employed	56	44	100
	Unemployed	73	27	100
Type of family	Joint	50	50	100
	Nuclear	65	35	100
Family h/o epilepsy	No	65	35	100
	Yes	57	43	100
Age at which you were diagnosed to have epilepsy	0-5yrs	75	25	100
	5-18yrs	70	30	100
	>18yrs	55	45	100
Type of therapy	Monotherapy	79	21	100
	Polytherapy	56	44	100
How frequently do you take medicine	OD	50	50	100
	BID	65	35	100
	TID	50	50	100
Family member reminding to take medicine	No	66	34	100
	Yes	59	41	100
Side effects affecting work	No	61	39	100
	Yes	69	31	100

- **History of noncompliance** It is found that only 10% compliance rate is present among the patients who are non-compliant in the past and 92% compliance rate is present among the patients who are not having history of non-compliance. This clearly states that history of non-compliance is the potential and major factor that is influencing the drug compliance. These results were similar with the study conducted by Vineetha J.R "A study to determine the drug compliance among people with epilepsy".

- **Expenditure** patients who had expenses less than Rs.500 shown to be more compliant (74%) than the patients whose expenses are high. Majority of the patients stated cost factor as the reason for non-compliance. The major reasons for noncompliance stated by the patients were cost factor (27%) and forgetfulness (18%) which was supported by a study conducted by Asawavichienjida (2003) to measure compliance with treatment of adult epilepsy in Thailand, having majority reasons for noncompliance were forgetfulness 16.1% and economic problem.[16]

- **Frequency of medication** Patients taking medicines twice a day were found to be more compliant than the patients taking medicines thrice a day. The result was supported by a study conducted by Gomes and Filho (1998) to assess medication taking behavior and drug self-regulation of people with epilepsy. Patients took the drug more than once in most cases (75.0%).[17]

- Our study says that 63% of patients never missed their dose, 48% of the patients had developed side effects which supported by a study by Buck and Jacoby (1997) to assess the factors influencing drug compliance with anti-epileptic therapy (72%) of patient said they never missed taking their medication and 50% patients reported AEDs side effects.[18]

- **Education** The patients who are educated seem to be more compliant, which implies knowledge about the drug effects on the life style may help the patients to overcome non-compliant nature. The result was like a study conducted by Joanne Eatock "Managing patient adherence and quality of life".[15]

- **Side effects** patients suffering from side effects were 59% compliant whereas patients not suffering from side effects were 68% compliant. It shows that presence of side effects may influence the drug compliance in patients. The results were like the study of "Determinants of compliance in Saudi epileptic patients" by Mohammad Abdul Jabbar.[19]

- **Duration of illness** Patients suffering from epilepsy for the duration of less than 10 years were more compliant (66%). But the compliance rate is shown to decrease among the patients who are suffering from more than 10 years (54%). This implies lesser the duration of illness greater the compliance rates. These were supported by "Handbook of health behavior Research-II Provider Determinants" by David.S. Gochman.[20]

- **Type of therapy** patients following monotherapy found to be more compliant (79%) than patients following polytherapy. These results were supported by Bruce Packham in the study of "How to improve compliance with AEDs".[21]

- The objectives of the study were achieved. The major factors influencing the drug compliance were found to be history of noncompliance, expenditure, frequency of medication, education, side effects, duration of illness, type of therapy. And depending on these factors the counseling was done. The patients were reassessed, and we found that majority of the patients who were non-compliant in the past denied stopping of medication. The compliance rate was increased by 29%.

Limitations

The study was conducted for a short period of time. The patients were not admitted in the hospital and so, the communication was difficult in the outpatient department. Many patients were not willing to answer to the questionnaires and were included in exclusion criteria.

Directions for the future study

Clinical Pharmacists should create awareness about the risks associated with non-adherence and help the patients understand the importance of drug compliance in seizure control. Similar study can be done in pediatric patients. Similar plan of analysis can be used to check other factors influencing drug compliance.

CONCLUSION

Among 60 (100%) patients, majority (47%) of the patients were found to be diagnosed with GTCS and 36% of sample with CPS. Most of the epilepsy patients fall under the age group between 21-40yrs. Among 29 (48%) patients who experienced side effects, majority (43%) suffered from drowsiness. It is found that 63% of the sample found to be compliant. Drug compliance was found to be influenced significantly by the factors like education ($P=0.5$), duration of illness ($P=0.5$), side effects ($P=0.25$), expenditure ($P=0.5$), type of therapy ($P=0.75$), frequency of medication ($P=0.25$). Factor that is found to be influencing the drug compliance levels to the greater extent was history of non-compliance. Among 21 patients who had history of non-compliance [P-value $0.95 > 0.05$ level of confidence], 90% were non-compliant in the present study. Patient counseling was done according to the factors influencing drug compliance in each patient. Awareness was created among all the patients and reassessment was done. It is found that 92% of sample denied stopping medication which is 29% more compliant rate than the initial stage. The study was conducted to measure drug compliance and to identify the major factors which helped in counseling the patients appropriately and thus, helped in decrease of noncompliance nature in epilepsy patients.

ACKNOWLEDGEMENT

CONFLICT OF INTEREST

The authors declare no conflicts of interest

ABBREVIATIONS

P- value: Probability value; **P:** Probability value; **AEDs:** Antiepileptic drugs; **ICD:** Informed consent document; **Rs.:** Rupees; **CPS:** Complex partial seizures; **GTCS:** Generalized tonic clonic seizures; **SE:** Status epilepticus.

SUMMARY

This study was conducted with the objectives to determine

the drug compliance in epilepsy patients and to find the major factors influencing the drug compliance. The study was conducted in a Tertiary care hospital with a sample size of 60 epilepsy patients. The patients were interviewed using a structured questionnaire. The factors influencing the drug compliance were found to be education, duration of illness, side effects, expenditure, type of therapy, frequency of medication and history of non-compliance. Patient counseling was done and awareness was created among every patient. On reassessment we found that, the study was helpful and the drug compliance rate was increased by 29% comparatively.

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