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A Study on Comparison of Management of Recurrent seizure among Epileptic patient in a Government Medical College Hospital

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Abstract

Introduction:

Epilepsy is a chronic neurological illness that causes frequent, unprovoked seizures. Even with significant progress in our knowledge of the pathophysiology of epilepsy and the availability of a wide variety of antiepileptic medicines (AEDs), many patients still find it difficult to achieve adequate seizure control. There is still a lack of high-quality prospective observational studies that comprehensively compare the efficacy, safety, and tolerability of various management regimens for recurrent seizures among epileptic patients, despite the availability of a wide range of therapeutic alternatives. By offering insightful information on treatment patterns, clinical outcomes, and factors influencing treatment decisions across a variety of patient populations, these studies play a critical role in bridging the gap between clinical research and actual clinical practice.

Methods and Material:

This was a prospective observational study conducted on 240 patients who were admitted with recurrent seizure disorder (drug withdrawal seizure disorder) in the Department of General Medicine at Tiruppur Medical College Hospital over a period of 6 months, following and satisfying the inclusion and exclusion criteria

Results:
There were 57 females (24%) and 183 males (76%) in the study population. The patients' ages were distributed as follows: 50 (21%) belonged to the 18–30 age group, 102 (42%) to the 31–45 age group, and 88 (37%) to the 46–65 age group. 32% of the study's patients were smokers, 4% were drinkers, and 9% said they smoked and drank. Most people (55%) didn't follow these routines. Seventy percent of the patients had generalised tonic-clonic seizures. Of the 240 patients, 65 (or 27%) reported missing doses, 110 (or 46%) showed inconsistent drug intake, and 65 (or 27%) had stopped taking their prescription entirely. The study showed a variety of pharmaceutical choices with sodium valproate being administered the most (20%), followed by carbamazepine (10%) and levetiracetam (18%). According to the study, 74% of instances were caused by drug withdrawal seizures, with breakthrough seizures accounting for 19% of cases and alcohol withdrawal seizures accounting for 7%. After discharge Seizures: Within a month following release, 96% of patients continued to be seizure-free. After treatment, 80.8 percent of patients were able to manage their seizures in 2 to 4 days, whereas 9.5% of patients needed 5 days to gain control.

Conclusion:
The study emphasised the value of individualised care for a range of age groups, the influence of lifestyle factors on the control of seizures, and the efficacy of phenytoin in the management of generalised seizures. Critical difficulties were managing withdrawal symptoms and adhering to medication regimens. The results of the study highlight the necessity of post-hospitalization care and customised treatment plans. Furthermore, the variety of prescription options and drug combinations provides guidance for medical professionals. This study adds to the continuing endeavour to better the treatment of epilepsy and, eventually, patient outcomes.

Keywords: Epielepsy, Medication adherence, phenytoin, levetiracetam, missed dose.

Introduction

Epilepsy is a chronic neurological illness that causes frequent, unprovoked seizures. It is a major global health concern for both sufferers and healthcare professionals. Epilepsy is one of the most prevalent neurological illnesses, affecting people of all ages, socioeconomic backgrounds, and geographical locations, with an estimated 65 million cases worldwide. Even with significant progress in our knowledge of the pathophysiology of epilepsy and the availability of a wide variety of antiepileptic medicines (AEDs), many patients still find it difficult to achieve adequate seizure control.[1,2,3]

In addition to having a significant negative influence on patients' quality of life, recurrent seizures can raise healthcare costs, social stigma, and healthcare use. A multidisciplinary strategy is necessary for the effective management of recurrent seizures. This approach should include correct diagnosis, appropriate treatment methods, regular monitoring of treatment response, and psychosocial needs assessment of the patients. However, the best course of action for treating recurrent seizures differs greatly from person to person and is impacted by a variety of factors, including the type of seizure, its aetiology, co-occurring conditions, drug tolerance, and patient preferences.[4,5,6]

Antiepileptic medications (AEDs) are the mainstay of treatment for epilepsy, with the goal of preventing seizure recurrence with the least amount of side effects possible. The arsenal of available AEDs has grown significantly over the last few decades, providing physicians with a wide range of pharmacological alternatives that differ in terms of their mechanisms of action, pharmacokinetic profiles, and side effect profiles. Despite this variation, a sizable fraction of individuals with epilepsy still suffer from recurrent seizures. This can be attributed to a number of factors, including poor treatment adherence, unpleasant side effects, medication resistance, or inadequate AED efficacy.[7,8,9]

Epilepsy patients require a customised, evidence-based approach to managing their recurring seizures. This approach should include both pharmaceutical and non-pharmacological interventions, and it should be tailored to the specific needs of each patient. In patients with drug-resistant epilepsy or contraindications to medication, non-pharmacological treatment

modalities—such as dietary therapies like the ketogenic diet, neurostimulation techniques like vagus nerve stimulation and responsive neurostimulation, and surgical interventions like resective surgery and laser interstitial thermal therapy—play crucial roles.[10,11]

There is still a lack of high-quality prospective observational studies that comprehensively compare the efficacy, safety, and tolerability of various management regimens for recurrent seizures among epileptic patients, despite the availability of a wide range of therapeutic alternatives. By offering insightful information on treatment patterns, clinical outcomes, and factors influencing treatment decisions across a variety of patient populations, these studies play a critical role in bridging the gap between clinical research and actual clinical practice.

In order to fill this knowledge vacuum, a thorough evaluation of the treatment of recurrent seizures in epileptic patients across a variety of therapeutic settings is being carried out in this prospective observational study.[12,13,14,15]

Aim

The primary aim of the study the Comparison of Management of recurrent seizure among epileptic patient in a Government Medical College Hospital.

Objectives:

1. To determine the percentage of recurrent cases admitted in the hospital.
2. To evaluate the various types of seizures among recurrent cases.
3. To evaluate the number of episodes of seizures after withdrawal and missed dose.
4. To determine the control of seizures (number of episodes) after initiation of phenytoin infusion.
5. To evaluate the total dose of phenytoin infusion among recurrent and breakthrough seizures.
6. To determine the time taken for control of seizure among withdrawal and breakthrough seizures.
7. To find the number of episodes of seizures after a month from discharge between both groups.
8. To compare the time taken for control of seizure among missed dose, irregular medication and completely stopped medication group.

Methodology

Ethical Approval: This study was reviewed and approved by the Institutional Human Ethical Committee (IHEC) of Government Medical College, Tiruppur, in accordance with the ethical standards of the institution and national guidelines.

- Reference Number: 3019/ME1/2023
- IHEC Registration Number: EC/NEW/INST/2022/3218
- Date of Approval: 07.07.2023
- Project Reference Number: 43/2023

Study Site: This research was carried out at Department of General Medicine, Government Medical College Hospital, Tiruppur.

Study Duration: The study was conducted for 6 months.

Sample Size: 240 Patients were enrolled into this study

Sample size calculation is done using a formula $n = z^2 \times p\,(1-\beta) / \Sigma^2$

$$= \frac{(1.96)^2 \times (0.05)\,(1-0.05)}{(0.05)^2}$$

$$= \frac{3.8416 \times (0.05 \times 0.95)}{0.0025}$$

$$= \frac{0.182476}{0.0025}$$

$$= 72.99\ (73)$$

$$= 73 \pm 10\%$$

$$= 73+7 = 80 \text{ Each group}$$

Complete : $73 \pm 7 = 80$
Missed dose : $73 \pm 7 = 80$
Irregular : $73 \pm 7 = 80$

Study Setting: This was a prospective observational study conducted on 240 patients who were admitted with recurrent seizure disorder (drug withdrawal seizure disorder) in the Department of General Medicine at Tiruppur Medical College Hospital over a period of 6 months, following and satisfying the inclusion and exclusion criteria.

Study Design: A prospective observational study

Study method: **A** case report form was used to collect the study specific details. Age, gender, previous medications details were collected. Patients were categorised on the basis of medication adherence as irregular drug consumption, missing doses, and completely stopped. Recurrence of seizures were evaluated among all the groups. Dose of different drugs used for treatment of seizures were determined. Discharge medications and time taken for control of seizures were also evaluated.

Study Criteria

Inclusion criteria:

- **Age:** >18 years (The recurrence is more reported in the adult patients in the previous studies, hence the study included only above 18 years of age group patients) [11].
- Patients of both genders
- Known seizure cases
- Dose missed
- Irregular medication of AED
- Withdrawal cases completely stopped

Exclusion criteria:

- New onset seizure cases
- Pregnant and lactating mothers.
- Patients with psychiatric conditions.

Data Collection

A review of medical records, patient interviews, and laboratory testing will all be used to gather data. Software for statistical analysis will be used to examine the gathered data. We have analyze the data using both inferential and descriptive statistics.

Statistical Analysis

After entering the data into a Microsoft Excel spreadsheet, basic statistical procedures were used to do statistical analysis and provide frequencies and percentages.

Results

1. Subject characteristics

Subject characteristics		No. Of patients	Percentage
Age	18-30 years	50	21%
	31-45 years	102	42%
	46-65 years	88	37%
Gender	Male	183	76%
	Female	57	24%
Habits	Smoker	76	32%
	Alcoholic	9	4%
	Smoker & Alcoholic	23	9%

Past Medications	Carbamazepine	12	5%
	Levetiracetam	43	18%
	Sodium valproate	49	20%
	Carbamazepine	24	10%
	T. Phenytoin 100mg	4	2%
	T. Topiramate 25mg	1	0.40%
	T.lacosamide 100mg	4	2%
	T.oxcarbazepine 300mg	2	0.80%
	T. levetiracetam 500mg, T.carbamazepine 200mg	1	0.40%
	T. Frusemide, T.Diazepam	1	0.40%
	T.lacosamide 100mg, T.sodiumvalproate 200mg	1	0.40%
	T.Sodium valproate (200mg), T.Diazepam(5mg)	1	0.40%
	T. Sodium valproate 200mg, T.carbamazepine 200mg	1	0.40%
	T. Carbamazepine (200mg), T. Sodium valproate(200mg)	1	0.40%
	T. Phenytoin 100mg, T. Sodium valproate, T.diazepam	1	0.40%

Table 1 demonstrates that of the 240 patients in our investigation, 50 (21%) belonged to the 18–30 age group, 102 (42%) to the 31–45 age group, and 88 (37%) to the 46–65 age group. Among the 240 patients in our investigation, 57 (24%) and 183 (76%) were female. In the provided data, the prevalence of males is higher.

Of the 240 patients in our study, 32% were smokers, 4% were drinkers, and 9% were both smokers and drinkers. 55% of respondents said they did not engage in these behaviours.

About 39%s of the 240 individuals in our study did not take their prescribed medicine as directed.

The most often used medications among those who took them were carbamazepine (10%), levetiracetam (18%), and sodium valproate (20%). The percentages of those who used the other prescriptions were smaller.

2. Classification of seizure

Classification of seizure		No. Of patients	Percentage
Type of seizure	Generalized tonic-clonic seizure	168	70%
	Generalized atonic seizure	16	6%
	Focal seizure	41	17%
	Generalized myoclonic seizure	12	5%
	Generalized absence seizure	1	0.41%
	Post traumatic epilepsy	1	0.41%
	Status epilepticus	1	0.41%
Diagnosis of seizure	Drug withdrawal seizure	179	74%
	Alcohol withdrawal seizure	16	7%
	Breakthrough Seizure	45	19%

Of the 240 patients that participated in our study, 70% of the cases had generalised tonic-clonic seizures. Seizures of different kinds, such as focal seizures (17%) and generalised atonic seizures (6%), affected the remaining individuals.

We noted a variety of seizure types in the subjects. Drug withdrawal seizures were the most common, making up 74% of cases. Breakthrough seizures came in second at 19%, and alcohol withdrawal at 7%.

3. Medication adherence and discontinuation of AEDS

Medication adherence and discontinuation of AEDS	No. Of patients	Percentage
Dose missed	65	27%
Irregular medication	110	46%
Completely stopped	65	27%

We saw different patterns of drug adherence in our 240-patient study. In particular, 110 patients (46%) showed irregular drug consumption, 65 patients (27%) reported missing doses, and 65 patients (27%) had entirely stopped taking their prescription medication.

4. Classification based on number of medications prescribed

Medication	No. Of patients	Percentage
Phenytoin	236	61%
Diazepam	60	15.50%
Levetiracetam	20	5%
Sodium valproate	26	7%
Carbamazepine	2	0.50%
Midazolam	43	11%

For the purpose of managing seizures, different drugs were provided to 240 individuals in our study. The most often prescribed drug, phenytoin, was given to 61% of the patients. Levetiracetam (5%), Midazolam (11%), Sodium valproate (7%), Diazepam (15.5%), and Carbamazepine (0.5%) were among the additional drugs taken by the patients.

5. Classification based on total dose of phenytoin

Medications	Dose	No. Of patients	Percentage
Phenytoin	400mg	1	0.41%
	600mg	25	10.50%
	800mg	14	6%
	900mg	53	22.40%
	1000mg	1	0.40%
	1200mg	124	52.50%
	1500mg	13	5.50%
	1800mg	5	2.10%
Diazepam	10mg	3	5.20%
	15mg	9	15.70%
	20mg	24	42.10%
	25mg	11	19.20%
	30mg	3	5.20%
	40mg	7	12.20%

levetiracetam	2000mg	1	5.20%
	3000mg	5	26.30%
	4000mg	9	47.30%
	4500mg	1	5.20%
	5000mg	1	5.20%
	6000mg	1	5.20%
	7500mg	1	5.20%
Sodium valproate	1200mg	6	23%
	1600mg	14	53.80%
	2000mg	2	7.60%
	2400mg	1	3.80%
	800mg	2	7.60%
	40ml	1	3.80%
carbamazepine	1200mg	1	50%
	1600mg	1	50%
Midazolam	10mg	3	14.20%
	15mg	4	19%
	20mg	6	28.50%
	25mg	1	4.70%
	6cc	1	4.70%
	8cc	3	14.20%
	10cc	1	4.70%
	16cc	1	4.70%
	24cc	1	4.70%

6. Classification based on number of episode after withdrawal and missed dose

No. Of episode after withdrawal and missed dose	No. Of patients	Percentage
1 episode	53	22%
2 episode	97	40.40%
3 episode	72	30%
4 episode	9	4%
5 episode	5	2%
6 episode	1	0.40%
7 episode	1	0.40%
10 episode	2	0.80%

The majority of the 240 patients in our study—53 patients, or 22 percent—had one episode, and 97 patients, or 40.4%, reported two episodes following withdrawal and a missed dosage. Thirty-two patients, or a significant portion, had three episodes; the remaining percentages of patients, or 0.4% to 0.8%, reported four to ten occurrences.

7. Classification based on control of seizure after initiation of phenytoin

Control of seizure after initiation of phenytoin	No .of patients	Percentage
Yes	225	94%
No	15	6%

Out of 240 patients, after starting phenytoin, 225 patients (94%) reported successful seizure control. 6% of patients still had seizures after starting phenytoin. Based on these statistics, phenytoin medication was able to control seizures in a significant majority of the trial participants.

8. Classification based on control of seizure after initiation of phenytoin

No. Of seizure episode after a month from discharge	No. Of patients	Percentage
Yes	10	4%
No	230	96%

Ten individuals (4%) out of the 240 patients in our study had seizures within a month of their discharge, while the other 230 patients (96%), did not have any seizures during that time.

9. Classification based on time taken for control of seizure

Time taken for control of seizure	No. Of patients	Percentage
2 days	23	9.50%
3 days	87	36.20%
4 days	107	44.50%
5 days	23	9.50%

In our study, 240 patients After receiving medication, the majority of patients—194 in total, or 80.8%—achieved seizure control in two to four days. It took five days for 23 individuals (9.5%) in a smaller cohort to get seizure control.

10. Classification based on discharge medication based

Medication	No. Of patients	Percentage
Phenytoin (100mg)	154	64%
Sodium valproate (200mg)	4	2%
Levitiracetam (500mg)	2	1%
Diazepam (5 mg)	1	0.41%
Phenytoin (100mg), Sodium valproate (200mg)	26	11%
Phenytoin (100mg), Diazepam (5 mg)	35	14%
Phenytoin (100mg), Levitiracetam (500mg)	9	4%
Sodium valproate (200mg), Diazepam (5 mg)	3	1%
Sodium valproate (200mg), Carbamazepine (200mg)	1	0.41%
Diazepam (5 mg), Levitiracetam (500mg)	2	1%
Phenytoin (100mg), Diazepam (5 mg), Sodium valproate (200mg)	3	1%

The most often prescribed drug in our 240-patient study was phenytoin (100 mg), which was given to 154 individuals (64% of the total). A lesser proportion of patients received prescriptions for other drugs; four patients (2%), two patients (1%), and one patient (0.41%) received 200 mg of sodium valproate, two patients received 500 mg of levitiracetam, and smaller groups of patients received different combinations of these drugs.

11. Classification based on combination of drug after control of seizure

Combination after control of seizure combination of drug after control of seizure	No. Of patient	Percentage
Phenytoin, Diazepam	35	44.30%
Phenytoin, Sodium Valproate	26	32.90%
Phenytoin, Levitiracetam	9	11.30%
Sodium Valproate, Diazepam	3	3.70%
Sodium Valproate, Carbamazepine	1	1.20%
Diazepam, Levitiracetam	2	2.50%
Phenytoin, Diazepam,Sodium Valproate	3	3.70%

Following the successful control of seizures, different combinations of drugs were provided to the 240 individuals in our study. For 35 patients (44.3%), phenytoin and diazepam was the most often used combination. Other combinations included 26 patients (32.9%) who had phenytoin with sodium valproate, and smaller patient groups received different combinations.

12. Classification based on combination of drug after control of seizure

Drugs	No. Of drugs	Percentage
Sodium valproate	49	33.70%
Carbamazepine	36	24.80%
Levetiracetam	42	28.90%
T. Phenytoin, T. Sodium valproate, T.diazepam	1	0.60%
T.lacosamide	4	2.70%
T. Carbamazepine, T. Sodium valproate	2	1.30%
T. Frusemide, T.diazepam	1	0.60%
T.lacosamide, T.sodiumvalproate	1	0.60%
T.sodium valproate,T.diazepam	1	0.60%
T. Phenytoin	4	2.70%
T. Topiramate	1	0.60%
T.oxcarbazepine	2	1.30%
T. Levetiracetam , T.Carbamazepine	1	0.60%

In our study of 240 patients, various medications were prescribed: Sodium valproate to 49 patients (33.7%). Carbamazepine to 36 patients (24.8%).Levetiracetam to 42 patients (28.9%).Other medications and combinations to smaller groups of patients, such as Phenytoin, Diazepam, Lacosamide, and more.

13. Comparison of medication adherence patterns and mean average days

Type of medication adherence	No of patients	Mean average days
Dose missed	65	3.58
Irregular medication	110	3.45
Completely stopped	65	4.07

Missed dose	Irregular	Completely stopped
n=65	n=110	n=65
3.58 ± 0.82	3.45 ± 0.76	4.07 ± 0.94
95% CI for mean		
3.38 to 3.79	3.31 to 3.59	3.84 to 4.31

Analyzed using Mann-Whitney U tests (Non-parametric test) for the three pairs of groups:

1. Missed dose vs. Irregular: P=0.37

Alternative Hypothesis (H1): There is a significant difference between the two groups.

2. Missed dose vs. Completely stopped: P=0.003

Alternative Hypothesis (H1): There is a significant difference between the two groups.

3. Irregular vs. Completely stopped: P<0.0001

Alternative Hypothesis (H1): There is a significant difference between the two groups.

The mean average number of days for controlling recurrent seizures was lower in the first two groups, "DOSE MISSED" and "IRREGULAR MEDICATION".

Between the patient groups with dose missed and irregular medication, there are no significant mean changes.

When compared to the other two groups, the group of 65 patients who were classified as "COMPLETELY STOPPED" had the longest mean average days for lowering recurrent seizures.

Discussion

There were 57 females (24%) and 183 males (76%) in the study population. The gender distribution in this study may be a reflection of the higher prevalence of epilepsy in men, with a sizable male majority. This work bears similarities to those of K Radhakrishnan et al.[16]

The patients' ages were distributed as follows: 50 (21%) belonged to the 18–30 age group, 102 (42%) to the 31–45 age group, and 88 (37%) to the 46–65 age group. This report emphasises the necessity for individualised care across different life stages by highlighting the range of ages impacted by recurrent seizures. This is similar to study conducted by Sarabjot Kaur et al.[17]

32% of the study's patients were smokers, 4% were drinkers, and 9% said they smoked and drank. Most people (55%) didn't follow these routines. This information emphasises how important it is to take lifestyle variables into account while managing epilepsy because habits can affect the control of seizures and the effectiveness of medication. This work has similarities to that of Barbara A. Dworetzky et al.[18]

Seventy percent of the patients had generalised tonic-clonic seizures. 94% of patients reported successful seizure control after starting phenytoin treatment, while 6% of patients still had seizures in spite of the medication. These findings demonstrate the frequency of generalised seizures

and the effectiveness of phenytoin in their management. This study bears similarities to that of Mohit Gupta1 et al.[19]

Of the 240 patients, 65 (or 27%) reported missing doses, 110 (or 46%) showed inconsistent drug intake, and 65 (or 27%) had stopped taking their prescription entirely. These findings draw attention to the crucial matter of medication adherence and the possible consequences of non-compliance on the control of seizures. This work bears similarities to those of Hanka Laue-Gizzi et al.[20]

The study showed a variety of pharmaceutical choices with sodium valproate being administered the most (20%), followed by carbamazepine (10%) and levetiracetam (18%). The percentage of people using other drugs was lower. The variety of prescriptions highlights the significance of customised treatment plans in the management of epilepsy. This work bears similarities to those of Homa Sadeghian et al.[21]

According to the study, 74% of instances were caused by drug withdrawal seizures, with breakthrough seizures accounting for 19% of cases and alcohol withdrawal seizures accounting for 7%. This information highlights how crucial it is to control medicine withdrawal in order to stop seizures from happening again. This work bears similarities to those of Xing Hua Tang et al.[22]

1200 mg of phenytoin was the most often prescribed dosage, administered to 52.5% of patients. This knowledge can help medical professionals decide on the best dosages to control seizures, resulting in more efficient therapy. This work bears similarities to those of Zahra Khoshdel et al.[23]

After discharge Seizures: Within a month following release, 96% of patients continued to be seizure-free. Eighty-eight percent of the patients were able to manage their seizures in two to four days, whereas nineteen percent needed five days. These results demonstrate how successful post-hospitalization therapy is at preserving seizure control. This work has similarities to those of Tone E.M. Medalen et al.[24]

After treatment, 80.8 percent of patients were able to manage their seizures in 2 to 4 days, whereas 9.5% of patients needed 5 days to gain control. With this information, medical professionals can help patients have reasonable expectations about when their treatments will be completed. This study bears similarities to that of Amiri-Nikpour MR et al.[25]

The investigation shed light on the drug combinations used to treat seizures. Phenytoin and Diazepam was the most often combined medication, accounting for 35 cases (44.3%), followed by Phenytoin and Sodium valproate for 26 patients (32.9%), and a variety of other combinations for smaller patient groups. Healthcare professionals can use this information to help them make well-informed decisions about combining therapies to improve seizure control. This work has similarities to those of Sarah J. Nevitt et al.[26]

Conclusion

We have gained important information from our observational study on the treatment of recurrent seizures in patients with epilepsy. The study emphasised the value of individualised care for a range of age groups, the influence of lifestyle factors on the control of seizures, and the efficacy of phenytoin in the management of generalised seizures. Critical difficulties were managing withdrawal symptoms and adhering to medication regimens. The results of the study highlight the necessity of post-hospitalization care and customised treatment plans. Furthermore, the variety of prescription options and drug combinations provides guidance for medical professionals. This study adds to the continuing endeavour to better the treatment of epilepsy and, eventually, patient outcomes.

Limitations

- The single-center design of the study might restrict its applicability.
- The sample size might be insufficient for a thorough subgroup analysis.
- Self-reports were used for data collection, which may have introduced bias.

- The limited 6-month study period limits long-term evaluation, and co-occurring disorders were not taken into account in this investigation.

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