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Original Research Article

An observational comparative study on the immediate, deferred, and no use of antiepileptics in the management of seizure

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ABSTRACT

Background: The rationale for starting AEDs in patients with seizure and early epilepsy is still unclear. The decision to start and stop the drugs in patients with single seizures remains controversial. This study aims to compare the efficacy, safety, and short-term outcome of the immediate, deferred, and no use of AEDs in patients presenting with seizure.

Methods This observational study, included 87 patients with either gender or age group with first or multiple seizures to investigate immediate, deferred, or no AED use. Detailed demographics, history, and diagnostic test reports were recorded. Drug use patterns and outcomes of seizure recurrence and safety were evaluated.

Results: Out of 87 patients (56 male, 31 female), there were 26 paediatrics, 47 adults, and 15 elderly. Immediate AED treatment was given to 75%, 16% deferred, and 9% received no/SOS AED. Levetiracetam was commonly prescribed (78% in ED, 86% in wards, 63% at discharge). For immediate AEDs: 49% had good seizure control, 25% had recurrence, and 9% had breakthrough seizures. Deferred AEDs showed 36% good control/recurrence and 7% breakthrough. Without AEDs: 63% had good control and 25% had recurrence. AEs were higher in the immediate AED group (42%) vs. deferred (15%).

Conclusions: The study indicates that immediate use of antiepileptic drugs (AEDs) reduces short-term seizure recurrence but may increase adverse effects. In cases of reversible causes, it may be best to forgo AEDs. Decisions regarding AED therapy should be tailored to the patient's preferences and risk considerations.

Keywords: Antiepileptics (AEDs), Immediate, Deferred, Seizure control, Recurrence

INTRODUCTION

A seizure, derived from the Latin term "sacire," which translates to "to take possession," refers to a temporary presentation of symptoms or signs resulting from abnormal, excessive, or synchronous neuronal activity within the brain. Understanding the underlying mechanisms of seizures is crucial for effective management and treatment in clinical practice.¹ The international league against epilepsy (ILAE) identifies three main types of seizures: partial, generalized, and unclassified. It is estimated that 5–10% of individuals will experience at least one seizure, with the highest prevalence among young children and older adults. Seizure disorders

affect about 50 million people globally, with India accounting for 10 to 20% of this burden, particularly impacting patients in rural and remote areas.² Epilepsy is characterized by a risk of recurring seizures due to a chronic underlying condition. While a person with a single seizure or seizures caused by treatable conditions may not be diagnosed with epilepsy, a single seizure with high recurrence risk features can confirm the diagnosis.¹

Antiepileptic drug (AED) therapy is the primary and most effective treatment option for the majority of patients with epilepsy. It is essential to classify the seizures accurately, as different antiepileptic medications demonstrate varying efficacy against specific seizure types. The primary

objective of antiepileptic treatment is unequivocal: to prevent seizures while minimizing side effects and ensuring a manageable treatment regimen. It is crucial to recognize that the decision to initiate medication after a single seizure can be contentious; however, immediate commencement of AED treatment is often unnecessary, particularly when an underlying cause can be effectively addressed.³

Anticonvulsant therapy may not always be necessary for patients experiencing a single seizure. The physician, patient, and family should make the decision to start treatment collaboratively, considering factors such as the risk of seizure recurrence, medication effectiveness, and potential side effects. Although most patients regain consciousness soon after a seizure, prolonged postictal states or incomplete recovery might necessitate hospitalization. Inpatient care is also necessary for any additional medical complications. It is vital to ensure thorough assessments and informed decisions that prioritize patient health and safety.⁴

Determining when to initiate antiepileptic drug (AED) treatment is crucial, particularly for patients who have experienced a single seizure or have mild symptoms. Evaluating the immediate risk of seizure recurrence and the long-term goal of achieving a two-year remission while improving quality of life is essential.⁵ Prompt treatment is necessary for acute symptomatic and provoked seizures caused by brain injuries. It's important to understand that using AEDs solely as a preventive measure for epilepsy is ineffective, and they should generally be discontinued within six months. In cases of seizures triggered by factors like alcohol withdrawal, avoiding these triggers is vital for better outcomes.⁶

Randomized controlled trials suggest that delaying treatment for a single unprovoked seizure increases the risk of early recurrence but results in similar long-term remission rates as starting treatment immediately. It's important to evaluate individual risks and benefits to understand the treatment's impact on quality of life. Observational studies also examine recurrence after the first tonic-clonic seizure, with rates ranging from 23% to 71% over 2 to 3 years. This variation is mainly due to differences in selection criteria and patient characteristics, particularly the time from the first seizure to study entry and the use of anticonvulsant treatment.⁷

This study aims to conduct a thorough evaluation and comparison of the efficacy and safety of three distinct approaches to AED administration in patients who present with seizures. The focus will be on assessing the immediate use of AEDs, the delayed administration, and the decision to refrain from their use altogether. By analyzing the short-term outcomes associated with each of these strategies, this research seeks to provide important insights that may inform best practices in the management of seizure episodes within clinical contexts. This study also seeks to improve guidelines for clinicians treating

seizures by taking into account the individual circumstances of patients.

METHODS

Study design

An observational comparative study was conducted in the emergency department (ED) and in-patient department of the paediatrics department, general medicine department, critical care unit, and neurology department of a tertiary care hospital.

Study place

The study was conducted in Bangalore Baptist Hospital, Bangalore, India.

Study duration

The study was conducted from January 2023 to October 2023.

Study size

A total of 87 patients were included in the study who met the inclusion criteria and given consent for participation

Inclusion criteria

Individuals of any age or sex who present with acute signs and symptoms of seizures were included in the study.

Exclusion criteria

However, individuals with a pre-existing diagnosis of epilepsy were not eligible, nor were those who had received antiepileptic drugs for prophylaxis. Additionally, individuals who had undergone neurosurgery were excluded to avoid confounding variables related to surgical interventions.

Study procedure

Data was collected using a pre-designed form, capturing demographics, comorbidities, medication history, inspection of seizure characteristics, and any known etiology through imaging and EEG. Seizures were classified, and a diagnosis of epilepsy was made when appropriate. Patients received comprehensive information about the study's benefits and risks.

Patients who consented were included in the study, while those who did not were excluded. Eligible patients were evaluated in the emergency department for immediate or deferred treatment and the necessary medications for their hospital stay and discharge. Risks and benefits were assessed based on seizure recurrence and adverse events,

using the prognostic index from the MESS trial to estimate recurrence risk.

Patients were systematically observed throughout treatment, and data from case records were entered into an Excel spreadsheet for evaluation of various clinical parameters. A clear and systematic percentage method was utilized to analyse and present the results.

RESULTS

The study involved a total of 87 participants of varying gender and age ranges. Among these, 56 were male and 31 were female, with ages ranging from 1 month to 86 years and the average age of the participants being 37. Looking at the age distribution of the participants, it was found that the majority of the patients i.e. 47 (54%) patients belonged to the adult age group followed by 25 (29%) patients in paediatrics group and 15 (17%) older adults (Table 1).

In a study encompassing 87 patients, new-onset generalized seizures emerged as the most frequently diagnosed type. The primary causes identified were infections (20 patients) and cerebral defects/deficits (13 patients). Additional significant causes included stroke (13 patients), scar epilepsy (3 patients), and haemorrhage (4 patients). Notably, in 15 cases, the cause of the seizure remained undetermined. The analysis revealed that 69% of the seizures were classified as provoked, while 31% were unprovoked. Additionally, metabolic causes were noted in 6 patients, with other causes contributing to a smaller proportion of cases. Overall, 15 patients were found to have no identifiable cause for their seizures (Table2).

The study revealed that antiepileptic drugs (AEDs) were administered to 91% of the patients involved. Among those

treated, 75% received immediate intervention, while 16% were provided with deferred treatment. Additionally, 9% of the patients either did not receive any AED treatment or were given on-demand (SOS) treatment, which accounted for 2% of the total.

When examining the data by seizure type-provoked or unprovoked-it was found that all 27 patients with unprovoked seizures received treatment, with 23 undergoing immediate administration and 4 receiving deferred intervention. In contrast, 8 patients diagnosed with provoked seizures did not receive treatment for the underlying curable cause (Table 3).

Levetiracetam was the most prescribed antiepileptic drug (AED) across all settings, with utilization rates of 78% in the emergency department (ED), 68% during inpatient treatment, and 72% at discharge. It was used for immediate management in 65 patients (74%) and for deferred management in 4 patients (5%). Levetiracetam was given alone or in combination with first-generation AEDs, including lorazepam 18 patients (21%), midazolam 14 patients (6%), phenytoin 7 patients (8%), and diazepam 7 patients (8%) (Figure 1).

The study assessed the outcomes of immediate, deferred, or no use of anti-epileptic drugs (AEDs) in 87 patients. Of these patients, 48% achieved good seizure control and remained seizure-free throughout the study period. In contrast, 26% experienced seizure recurrence, and five patients died, although seizures were not the primary cause of death. The results showed that the seizure control was effective in patients who received AEDs immediately, whereas the recurrence rate was higher in those who delayed treatment (Figure 2).

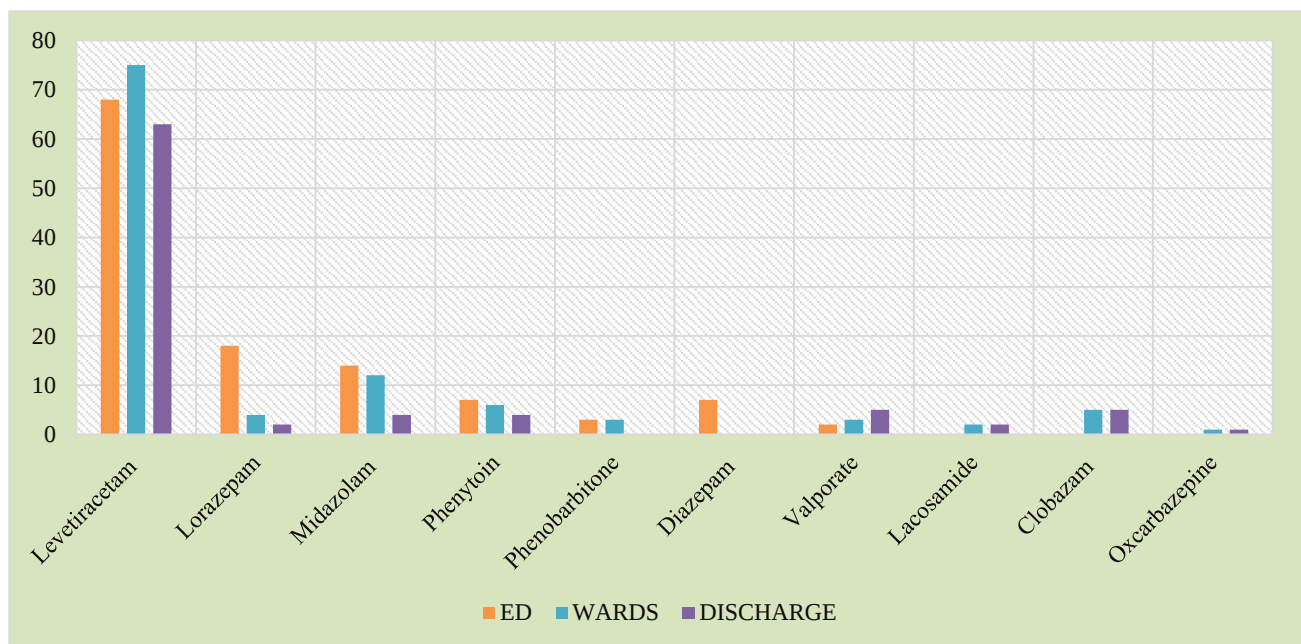


Figure 1: The usage patterns of AEDs (antiepileptic drugs) across various hospital settings.

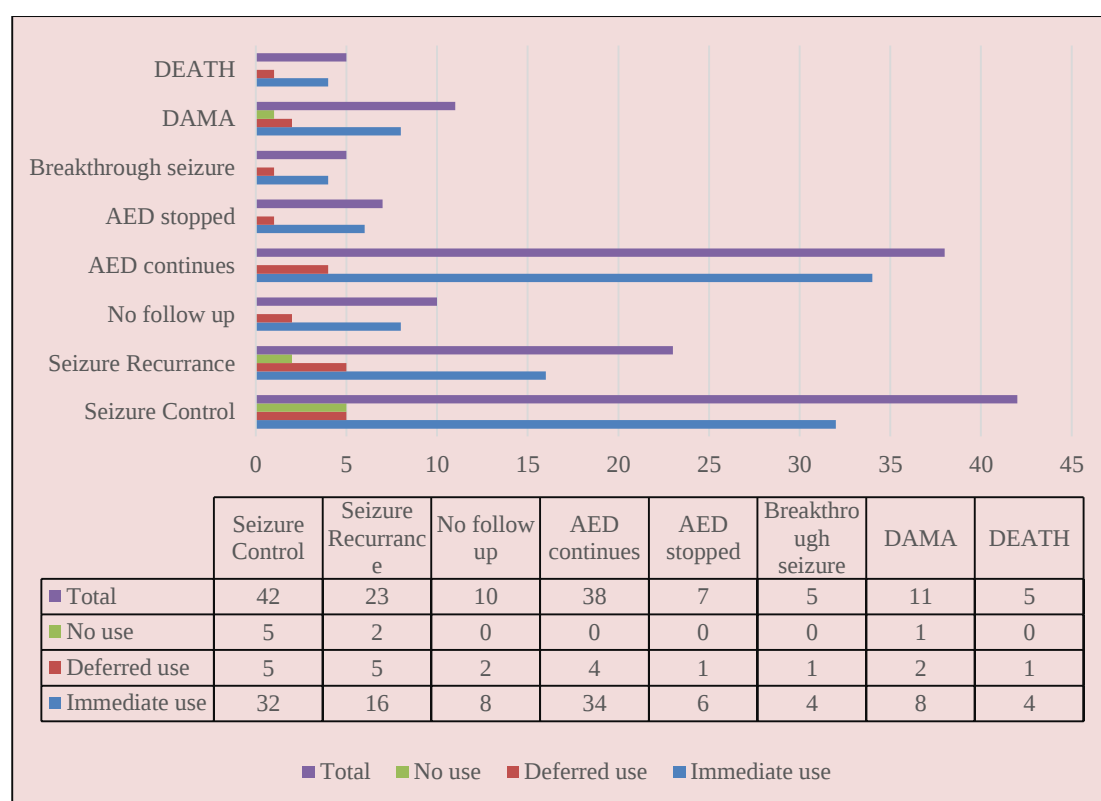


Figure 2: Comparison of the outcome of the immediate, deferred, and no use of AEDs in patients with seizure.

A comprehensive risk assessment based on the scores on the prognostic index for recurrence from the MESS trial of 87 patients showed that 83% had a medium to high risk of seizure recurrence (46% medium, 37% high), while 21% had a low risk. During the study, 23 patients (26%) experienced recurrence. The number of adverse events was

higher during immediate use of the AED at 27 cases, compared to 2 cases during deferred use. Most AEs were minor and did not require dosage adjustments. One patient developed Stevens-Johnson syndrome (SJS), leading to the discontinuation of phenytoin and its replacement with other AEDs (Table 4).

Table 1: Age-gender distribution of patients included in the study.

Age group	No. of patients			Mean±SD
	Male	Female	Total	
Paediatrics (1 month-17 years)	17	8	25 (29%)	6.01±5.07
Adults (18 years-64 years)	31	16	47 (54%)	42.34±15.55
Older adults (65 or older)	8	7	15 (17%)	73.2±6.63
Total	56 (64%)	31 (36%)	87 (100%)	37.22±25.82

Table 2: Patient distribution by seizure cause.

Causes	Provoked (60)	Unprovoked (27)	Total
Metabolic	6	0	6
Infection	18	2	20
Alcohol	3	0	3
scar epilepsy	0	3	3
Unknown	3	12	15
Eclampsia	1	0	1
Genetic/ Autoimmune	2	2	4
Infantile spasm	0	2	2
Syncope	1	2	3
CVA	12	1	13
Haemorrhage	4	0	4

Continued.

Causes	Provoked (60)	Unprovoked (27)	Total
Other, cerebral defects/ deficit	10	3	13
Total	60 (69%)	27 (31%)	87 (100%)

Table 3: AEDs usage patterns based on seizure type: provoked and unprovoked.

Seizure	Immediate use	Deferred use	No use	SOS
Provoked	42	10	6	2
Unprovoked	23	4	0	0
Total	65 (75%)	14 (16%)	6 (7%)	2 (2%)

Table 4: Adverse events occurring in patients during drug use.

AE	No. of patient			Severity	Action taken
	Total	Immediate	Deferred		
Constipation	2	2	0	Mild	None
Headache	9	9	0	Mild	None
Fatigue	4	0	0	Mild	None
Loose stool	1	1	0	Mild	None
Agitation	1	1	0	Mild	None
SJS	1	0	1	Severe	Phenytoin withdrawn
Weakness	1	1	0	Mild	None
Confusion	1	1	0	Mild	None
Dizziness	2	2	0	Mild	None
Giddiness	2	2	0	Mild	None
Tingling	1	0	1	Mild	None
Backache	1	1	0	Mild	None
Drowsiness	2	2	0	Moderate	Levetiracetam stopped in one
Epigastric pain	1	1	0	Mild	None

DISCUSSION

In this study, a total of 87 eligible patients, encompassing a diverse range of ages and genders, were evaluated for the risks and benefits associated with the early versus delayed administration of antiepileptic drugs (AEDs). The assessment focused on factors such as seizure control, recurrence rates, and adverse events. Of the participants, 56 were male and 31 were female, with ages spanning from 1 month to 86 years. A majority of the participants (54%) were 18 years of age or older. These findings are consistent with the studies conducted by Pal A et al, and B Yogesh et al, which similarly indicated a predominance of males within the adult age group.^{8,9} Overall, these findings demonstrate the importance of considering gender and age as key factors while assessing the patient distribution and healthcare utilization.

This study found that 75% of patients received immediate treatment, while 16% received deferred treatment, and 9% did not receive any AED treatment. The most commonly used and prescribed drug in this study was levetiracetam, accounting for 86% of prescriptions across all hospital settings. This finding aligns with an observational study involving 380 patients, which reported that 73% received

immediate treatment and 27% received deferred treatment regarding the initiation of AEDs. However, the choice of AEDs differed in that study, with valproate prescribed to 49% of patients, carbamazepine to 18%, and phenytoin to 17%. Newer AEDs were used in 15% of cases, primarily lamotrigine (8%) and levetiracetam (6%), as noted in the research conducted by Sameer et al.¹⁰ In the study, short-term seizure control was observed in 49% of patients who used antiepileptic drugs (AEDs) immediately, compared to 36% of those who delayed treatment and 63% of non-users. During the study, 23 out of the total 87 patients experienced a seizure recurrence, resulting in an overall recurrence rate of 26%. This included 16 patients (25%) of the immediate treatment group, 5 patients (35%) of the deferred treatment group, and 2 patients (23%) of the non-treatment group. Another study indicated that after one year, the recurrence rates were 57% for those who delayed treatment, while immediate treatment resulted in lower recurrence rates of 38%.¹⁰

During the course of the study, it was observed that out of all the cases, 5 patients experienced a breakthrough seizure. This was found to be mostly due to skipping or missing the dose of the medication. However, it is worth noting that the drug selection, in terms of dose and duration, was deemed

appropriate. These findings underscore the importance of regular assessments to monitor the risk of seizure recurrence and ensure appropriate treatment and care.

The immediate use of AEDs was associated with a higher risk of adverse effects, with 27 cases reported in the immediate treatment group compared to just 2 cases in the delayed treatment group, as noted by Mason et al, in his study.¹¹ More patients in the immediate group reported adverse events that were likely related to treatment, although these side effects were rarely severe or life-threatening. Interestingly, the patients who did not use AEDs had a significantly better outcome. Among them, 63% remained seizure-free, and only 25% experienced seizure recurrence. In this group, the causes of seizure recurrence were curable, which indicates that the use of AEDs was not necessary. This finding highlights the importance of carefully considering the use of AEDs in patients who may not require them. Antiepileptic drugs (AEDs) help most patients stay seizure-free, but side effects can reduce adherence. While older medications like phenytoin and carbamazepine are still used, newer options like lamotrigine and levetiracetam are preferred for their better tolerance.

Furthermore, the need for multiple medications may arise, increasing the risk of drug interactions and financial strain. When starting AEDs therapy, it's important to weigh the recurrence risk benefits against potential side effects. Several newer AEDs are effective, well-tolerated, and safe, enabling early long-term treatment.¹² The patient's perspective is essential when deciding whether to start antiepileptic drug (AED) treatment after a first seizure. Their social, psychological, and emotional profile will greatly influence the final decision.¹³ The decision to begin antiepileptic drug treatment after a first seizure is controversial and often guided by tradition rather than evidence. A review highlights the need for further studies on the impact of starting and stopping treatment on epilepsy's clinical course and prognosis.

It's important to recognize that every study has limitations and boundaries that should be considered as constructive aspects of the research process. In this case, the study was conducted over a short duration with a small sample size, and epilepsy and seizures are often underreported. Additionally, a thorough investigation was insufficient to reach a final diagnosis, there was a failure to follow up with patients, communication barriers existed, and there was a lack of proper guidelines for seizure treatment.

CONCLUSION

The study shows that using antiepileptic drugs (AEDs) immediately offers better seizure control and reduces recurrence risk compared to delaying treatment, which increases the chances of seizures returning. However, immediate AED use may also carry higher risks of side effects. Provoked seizures, which arise from acute illnesses, usually resolve with appropriate treatment, so

long-term AED use may not be needed. Therefore, when treating patients with uncertain conditions, it's important to balance the benefits of seizure prevention against potential side effects. Considering the effectiveness, tolerability, safety, and drug interactions is essential for successful long-term treatment. Additionally, involving the patient's perspective in the decision to start AED treatment after a first seizure is critical.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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