



Drug Utilization Review of Antiepileptic Medications in Pediatric Patients: Insights from a Rural Secondary Care Hospital

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ABSTRACT:

Introduction: Seizure is one of the most common neurological disorders in pediatric populations, often requiring management with antiepileptic drugs (AEDs). Drug utilization studies play a crucial role in evaluating prescribing patterns, optimizing therapy, and improving clinical outcomes. This study aims to assess AED utilization in pediatric patients at a rural secondary care hospital, providing insights into current treatment effectiveness and safety.

Aim: The study aims to evaluate the prescribing patterns of AEDs in pediatric patients and analyze the safety and efficacy of various AED regimens in a rural healthcare setting.

Study Design: A prospective, observational study involving pediatric inpatients at a rural secondary care hospital was conducted over a six-month period, from December 2023 to May 2024.

Methodology: The study includes 120 pediatric patients aged 1–14 who are prescribed AEDs. Data are collected on demographics, seizure types, AED regimens (monotherapy, dual therapy, polytherapy), and adverse drug reactions (ADRs). The causality of ADRs is assessed using the Naranjo Causality Assessment Scale. Statistical analysis is performed using SPSS V.17 to identify patterns and associations between seizure types, drug utilization, and clinical outcomes.

Results: The results show that 51% of the patients are aged 1–5 years, with tonic-clonic seizures being the most common type (23.3%). Clobazam is the most frequently prescribed AED (49%), followed by sodium valproate (34%) and midazolam (36%). Monotherapy is administered to 32% of the patients, dual therapy to 54%, and polytherapy to 8%. A seizure-free rate of 87% is observed, while 10% of patients report 1–2 episodes, and 3% experience more than two episodes. ADRs, primarily associated with phenytoin, include ataxia, rashes, and lymphadenopathy, leading to drug discontinuation in some cases.

Conclusion: This study highlights the prevalent use of Clobazam and the efficacy of dual therapy in managing pediatric seizures. The findings underscore the importance of continuous monitoring for ADRs, particularly in patients receiving phenytoin, and the role of clinical pharmacists in optimizing therapy. The high seizure-free rate suggests that AED regimens, when tailored to seizure type, can significantly improve outcomes in pediatric populations, particularly in rural healthcare settings.

1. Introduction

Seizure is the most prevalently affecting neurological disorder in childhood. ⁽¹⁾ Seizures are defined by short episodes of involuntary motion. ⁽²⁾ A lower seizure

threshold is associated with higher excitability in the cortical and subcortical motor system's central neurons. The disorder is characterized principally by unusual motor activity, such as tonic, tonic-clonic, absence, and



myoclonic seizures that occur along with or without loss of consciousness.⁽³⁾ Approximately 4-10% of children experience at least one seizure during the first 16 years of life. With a declining frequency in older children, the prevalence is highest in children under the age of three.⁽²⁾ Childhood epilepsies are a diverse set of disorders with widely varying management approaches, diagnostic standards, and assessments.⁽⁴⁾ Antiepileptic medications are used for the symptomatic treatment of various kinds of epilepsy.⁽³⁾ Preventing irreversible damage to neural cells is the primary objective of antiepileptic therapy.⁽⁵⁾ The treatment agents must elevate the seizure threshold without influencing motor excitability. Antiepileptic drug utilization studies are critical for optimizing pharmacological therapy and drug control.⁽³⁾ The proper antiepileptic drug (AED) is determined by the type of seizure and the patient's age.⁽⁶⁾ New treatments for epilepsy offer improved quality of life. However, a steady rise in the possibilities makes selecting the best treatment or combination of treatments far more challenging.⁽⁷⁾ When selecting from the expanding array of pharmaceuticals, physicians frequently lack comparative data, which leads to significant variation in treatment practices. Given the significantly lower number of drug trials conducted in children than in adults, the absence of comparative efficacy data is especially apparent for pediatric patients.⁽⁸⁾ Monotherapy is typically the first line of treatment due to its reduced drug interactions and adverse effects, lower cost, improved tolerability, medication adherence, and quality of life. Even with advancements in epilepsy treatment, 30–40% of patients cannot be managed with a single AED.⁽⁶⁾ Polytherapy is frequently used to treat different types of epilepsy, despite its increased side effects.⁽⁹⁾ A drug utilization study provides both quantitative and qualitative information about the conditions of drug use as well as the users of a particular class of drugs. Drug utilization studies are a valuable tool for interpreting, addressing, and advocating for sensible medication prescription, distribution, and administration.⁽¹⁰⁾ They establish a solid sociomedical and health-economic foundation for clinical decision-making.⁽¹¹⁾ Hence our study is designed to analyse the AED utilization among various types of seizures and their clinical outcomes.

2. Aim

The study aimed to evaluate antiepileptic drug utilization patterns and assess the effectiveness and safety of

different therapies in pediatric patients at a rural secondary care hospital.

Ethical approval

Ethical approval was obtained from the Institutional Ethics Committee (IEC) ECR\319\Inst\TN/2013/RR-19. All the study patients signed a written informed consent form before their recruitment into the study.

3. Statistical analysis

The data collected during the study were formulated into a master chart using Microsoft Office Excel, and statistical analysis was performed using the statistical software package SPSS V.17 for Windows.

4. Methods

This prospective observational study was conducted in 120 patients over six months from December 2023 to May 2024. All prescriptions of the inpatients were analysed and recorded on our case record forms. The data were retrieved from their prescription and the patient's medical records by explaining the study protocol to their caretakers. The data collected were demographic details, type of seizure, rate and duration of seizure, type of antiepileptic prescribed, and ADR data. The study evaluated AED utilization by categorizing patients according to the seizure type and the prescribed AED regimen (monotherapy, dual therapy, or polytherapy). Patterns of AED use, including the frequency of prescribed drugs and their combinations, were assessed. ADRs were identified and assessed using the Naranjo Causality Assessment Scale to establish causality. Management of ADRs, including any changes in therapy (e.g., discontinuation of AEDs), was recorded.

The study received institutional ethics committee approval before its initiation, and informed consent was obtained from all patient's caretakers. Patients who are between 1 and 14 years of age, inpatients of both sexes who are prescribed antiepileptic medications during their hospital stay, and patients who are willing to participate. Patients who are attending the outpatient department and patients who are not willing to participate.

5. Results

Out of 120 patients included in the study, there is no significant difference seen among the gender distribution, as the male patients constitute about 53% (n



= 64) and the female patients about 47% (n = 56). The highest prevalence of seizures was found in the age group of 1–5, which comprises nearly 51% (n = 61), and the lower prevalence was found in the population of age group 11–14, as it contributes 23% (n = 28) of the total population.

Table 1 Demographic data

		N (%)
Gender	Male	64(53%)
	Female	56(47%)
Age wise distribution	1 – 5	61(51%)
	6 – 10	31(26%)
	11 – 14	28(23%)

Table 2: Distribution of seizure type among the population

		N (%)
Types of seizure	Simple febrile	26(22%)
	Complex febrile	21(17.4%)
	Simple partial	18(15%)
	Complex partial	9(7.5%)
	Absence	8(6.6%)
	Atonic	2(1.6%)
	Status epilepticus	6(5%)
	Tonic clonic	28(23.3%)
	Myoclonic	2(1.6%)

There were nine types of seizures observed during our course of study. Among them, tonic clonic seizures (n = 28) were the most widely observed type of seizures, followed by simple febrile seizures (n = 26). The most rarely observed seizure types are atonic and myoclonic seizures.

Table 3: Drug distribution according to type of seizure

Seizure Type	Clobazam	Sodium Valproate	Phenobarbitone	Midazolam	Phenytoin	Carbamazepine	Levetiracetam
Simple Febrile	✓						
Complex Febrile	✓			✓			
Simple Partial	✓	✓		✓			✓
Complex Partial	✓	✓	✓		✓		
Absence	✓		✓	✓			
Atonic				✓			
Myoclonic Seizure	✓	✓					
Status Epilepticus		✓		✓	✓	✓	✓
Tonic Clonic		✓	✓	✓	✓	✓	✓

From this table, it is found that for simple febrile and complex febrile seizures, Clobazam is the most commonly prescribed drug to all patients. Sodium valproate and phenytoin were commonly prescribed in tonic-clonic, status epilepticus, simple, and complex partial seizures. Clobazam is the highly prescribed

monotherapy drug, followed by sodium valproate and phenytoin, which are the highly prescribed combined dual therapy drugs. Dual therapy was observed in 54% of the population, followed by monotherapy, which was observed in 32% of the population mainly on simple febrile and atonic seizures. Triple therapy was observed



in 8 patients, and polytherapy was observed in 6 patients. A variety of combinations of AED usage were observed in status epilepticus and tonic clonic seizures, whereas atonic seizures, myoclonic seizures, and simple and complex febrile seizures followed the same drug utilization pattern in all the patients.

Table 4: Drug Utilization

		N (%)
Drug distribution	Clobazam	59(49.2%)
	Sodium Valproate	41(34.2%)
	Phenobarbitone	14(11.7%)
	Midazolam	43(35.8%)
	Phenytoin	35(29.2%)
	Carbamazepine	5(4.2%)
	Levitracetam	20(16.7%)

From this table, we observed that Clobazam (27%) was the widely prescribed AED in our study, followed by Midazolam (20%), while Carbamazepine (2%) was the underutilized drug among all AEDs.

Table 5: Choice of therapy for different types of seizures

Types of seizure	Mono therapy	Dual-Therapy	Poly-therapy
Simple Febrile	26(22%)		
Complex Febrile		21(18%)	
Simple Partial	12(10%)	6(5%)	
Complex Partial		8(7%)	1(0.8%)
Absence		4(3%)	4(3%)
Atonic		2(2%)	
Status Epilepticus			6(5%)

Tonic Clonic	1(0.8%)	22(18%)	5(4%)
Myoclonic		2(2%)	

Monotherapy is the preferred treatment option for patients with simple febrile and myoclonic seizures. Dual antiepileptic therapy has been approached for treatment of most types of seizures observed in our study. Polytherapy is not commonly utilized in treatment, as it is applied only to patients with varying degrees of seizure severity. Polytherapy has been identified as the sole treatment option for status epilepticus. Our results indicate that tonic-clonic seizures can be managed through monotherapy (n = 1), dual therapy (n = 22), and polytherapy (n = 5).

Adverse drug reactions

The most commonly observed side effects are ataxia (n = 2), rashes (n = 1), and lymphadenopathy (n = 1) which were reported in patients taking phenytoin. The ADRs were seen in the patient's taking phenytoin, which was confirmed by the Naranjo causality assessment scale, and phenytoin was discontinued from the patient's regimen, and to replace Phenytoin, sodium valproate was included in the therapy.

Table 6: Effectiveness of treatment

		N (%)
Drug efficacy	Seizure Free	104(87%)
	1 – 2 episodes	12(10%)
	>2 episodes	4(3%)

From this table, it is shown approximately 87% of the 120 patients who came for follow-up on OP reviews (n = 104) were seizure-free during our study; 12 patients reported having one or two seizures, and 4 patients reported having more than two seizures.

6. Discussion

The main goal of drug utilization research is to promote rational drug use. Drug utilization research is crucial for patients with chronic conditions like epilepsy since these people often have lifetime dependence on drugs. Furthermore, polytherapy is necessary for both the comorbid ailments and the disease itself in these cases. The primary disadvantages of polytherapy include side



effects, medication interactions, and increased financial strain on the patients. In such cases, it is necessary to understand the numerous prescribing indicators.⁽¹²⁾

The total number of patients included in this prospective study was 120 during the period of December 2023 to May 2024 at a secondary care hospital. In this study, we found no statistically significant age differences based on seizure exposure, as the number of male and female participants was approximately equal. We found that seizures were more commonly reported in the 1–5 age group, as these patients were more likely to experience febrile seizures. This finding is consistent with those of Hemal J. Dholakia et al. and Kousalya K et al., who also observed that the most prevalent pediatric age group diagnosed with epilepsy was under the age of five.^(13,14)

Among the various types of seizure presentations observed during the course of the study, generalized tonic-clonic seizures were the most commonly observed seizure type among the study population, which is consistent with the findings of Jayant Rai et al. and Habib M et al., who reported that the most common seizure type observed was generalized tonic-clonic seizures in the epileptic patients in their study.^(15,16)

Based on our investigation, we discovered that Clobazam was the most often prescribed AED because the majority of the patients had been diagnosed with both simple and complex febrile seizures. For treating both kinds of febrile seizures, clobazam continues to be the gold standard. Among all the prescribed AEDs, sodium valproate is the most often used medication, followed by clobazam. Sodium valproate continues to be the primary medication of choice for treating a variety of seizures since it has demonstrated improved treatment outcomes in the management of epilepsies. We found that sodium valproate is more frequently prescribed than benzodiazepines, contrary to studies by Princy Christian et al. and Keerthana Y et al. that claimed phenytoin was the most frequently prescribed medicine after benzodiazepines.^(2,17) Abhisek Pal et al.'s study report corroborated our study's findings, stating that sodium valproate was the most frequently utilized AED, followed by phenytoin.⁽⁹⁾ Sodium valproate exhibits sodium channel blocking activity, restricting persistent, high-frequency repetitive firing and diminishing calcium conductance (T-type calcium channels), which attenuates thalamocortical oscillations.⁽¹⁸⁾

Monotherapy was utilized to treat seizures in 39 patients (32%), while dual therapy was commonly employed to treat the majority of seizure presentations, with 65 patients (54%) receiving dual antiepileptic medications. Our study's findings differed from earlier research by Mounika Anthem et al. and Rochat P et al., who stated that monotherapy was the most often prescribed course of treatment for epilepsy.^(19,20) A total of 317 AEDs were prescribed over the study period, corresponding to an average of 1.8 AEDs per patient.

The most commonly observed side effects are ataxia, rashes, and lymphadenopathy that were reported in patients taking phenytoin. The ADRs were seen in the patient's taking phenytoin, which was confirmed by the Naranjo causality assessment scale, and phenytoin was discontinued from the patient's regimen, and to replace Phenytoin, sodium valproate was included in the therapy. The seizure-free period observed in 87% of the population shows successful optimization of the therapy. The findings suggest a significant role for clinical pharmacists in monitoring AED therapy, optimizing treatment regimens, and minimizing ADRs. This study's findings can suggest better treatment protocols and guide the rational use of AEDs in pediatric seizure management.

7. Conclusion

In this study, it was evident that the prevalence of seizures among the age group 1–5 years was high, and the most commonly seen type of seizure was tonic-clonic. Highly distributed and prescribed drug in this secondary care hospital is Clobazam, and most of the ADR's seen in patients taking Phenytoin. The ADRs observed are very low. The present study provides valuable data on utilization patterns of AEDs. Dual therapy was the most commonly prescribed regimen, with Clobazam, sodium valproate, and phenytoin being the most preferred drugs of choice in combination therapy. ADRs were observed primarily with phenytoin, indicating the need for careful monitoring and drug management in the pediatric population. A seizure-free rate of 87% reflects the efficiency of the prescribed AED regimen. Clinical pharmacists have a crucial role in conducting drug utilization studies that help in comparing the ongoing regimen with the standard treatment guidelines as it promotes the rational use of drugs and to minimize or control the incidence of ADRs.



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