Asian Journal of Hospital Pharmacy
Available at www.ajhp.online ISSN: 2583-0724

# Review on pediatric seizures - a prospective study on drug utilization pattern and its outcome

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*Received: 22 April 2022 Revised: 06 May 2022 Accepted: 14 June 2022*

**Abstract**

Objectives: The objective of this study is to evaluate the drug utilization pattern and to observe possible treatment outcomes.

Methods: A Non-experimental prospective observational study has been carried out in tertiary care hospital for a period of six months. A total number of 181 pediatric inpatients of age 1- 14 years with seizures were included and evaluated. The patient's case history was collected based on a data collection form designed for the study.

Results: In our study, we observed that female patients are more prevalent. Prevalence of seizures is high among the age group 1-5years and low among 11-14 years. Tonic-clonic (51.3%) types of seizures were commonly observed, followed by febrile seizures (19%). Phenytoin is the most prescribed drug followed by sodium valproate. Monotherapy is observed mostly. The outcome of the therapy is measured by seizure-free period, among which seizure-free observed are more than 74.1%. The incidence of ADRs in the study group is less (6.6%) and phenytoin is the drug with more number of ADRs. Medication adherence is measured in known epileptic patients (n=67) using MMAS, medium adherence seems to be more (49%).

Conclusion: This study strongly highlights that the Clinical pharmacist has a pivotal role in conducting drug utilization studies that help in comparing the ongoing regimen with the standard treatment guidelines so as to promote the stupendously rational use of drugs and to minimize or control the incidence of ADRs.

*Keywords: Drug utilization, seizure, anti-epileptics, Morisky's scale.*



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DOI: https://doi.org/10.38022/ajhp.v2i2.50

## Introduction

Epilepsy is the most common neurological disorder observed in pediatrics which has to be diagnosed to choose a proper antiepileptic and has to be used for appropriate duration with proper monitoring as they are potential [1,2]. Untreated pediatric epilepsy may result in MR and deaths and hence the cause of epilepsy and type of epilepsy and AED for it has to be properly selected for better outcome [3, 4]. There are many AED's available now in market and are broadly categorized as conventional AED's and newer AED's [2]. Based on risk to benefit ratio and economic status of a country, type of seizure AED's are selected, also as they have many side effects due to their potential action and however children are at risk, dosing, frequency, duration are to be properly opted [2,3,4]. Phenytoin and valproate are most frequently selected AED's in India. Adherence play a major role for a beneficial outcome, hence it has to be monitored. For better adherence, cost effective therapy and to minimize drug interaction and side effects monotherapy is to be chosen [4, 5]. This is a prospective study on drug utilization pattern and outcomes of AEDs in pediatric seizures in a tertiary care hospital. Drug

utilization patterns can increase understanding of the rational drug use in pediatric seizures and its outcomes [6, 7, 8].

MATERIALS AND METHOD

## Study Material

A Non-experimental prospective observational study has been carried out in tertiary care hospital for a period of six months. The study material consists of a data collection form approved by the ethical committee of the institution, and strict confidentiality was assured for all collected data.

**Data Collection and analysis**

The data is retrieved from the prescription and the patient's medical records by explaining the study protocol and receiving informed consent from the patient care taker. It includes the details like patient demographics (age and gender), type and etiology of seizures, past medical and medication history, and Co-morbidities. A detailed history was taken regarding the time and duration of attack, symptoms, and factors which may trigger seizures, a total number of seizure episodes, AED data (i.e. type of prescription and dosage regimen), tests performed, ADR data, medication adherence data, and admission status (admitted because of epileptic seizures, ADR related to AED or other reason). The epileptic seizures were classified according to the International Classification of Epileptic Seizures and possible etiologies were documented. Apart from the classification (International Classification of Epileptic Seizures), refractory seizers were also included. The patients were assessed for medication adherence behavior by using Morisky's medication adherence scale. All patients included in the study are followed up in OP reviews/ through phone calls, at least twice during the study period for the outcome (seizure-free period, ADR). From the data, results were drawn using suitable statistical methods.

Inclusion Criteria

The study population was limited to:

- Age group: 1-14 years.
- Inpatients with seizures of both sexes, who are prescribed with the anti-epileptic drug during their hospital stay.
- Patients who are willing to co-operate.

**Exclusion Criteria**

- Old cases of seizures who are attending to the Outpatient department.
- Patients who are not willing to participate in the study.

## Results

The total numbers of patients admitted with seizures from 1st August 2021 to 31st December 2021 were 181.

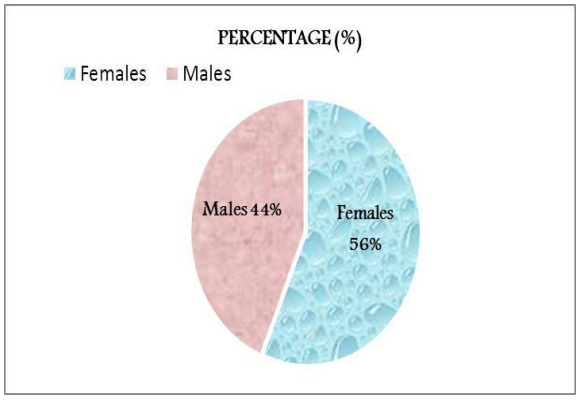


Fig 01: Gender Wise Distribution of Study Population

## Population

Out of 181 cases, 79 cases (44%) were males, 102 cases (56%) were females. Females were found to be in high number compared with males.

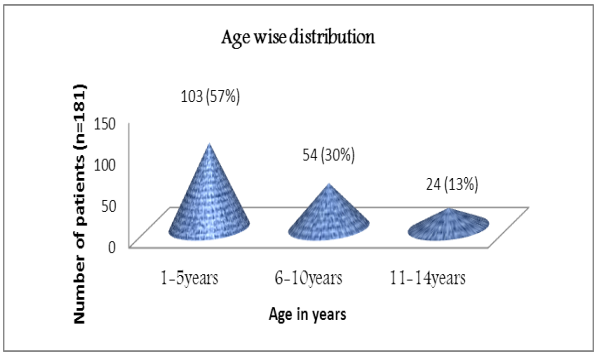


Fig 02: Age Wise Distribution of Study Population

The highest incidence of seizures was found in the age group 1-5 years and least in the age group 11-14 years, Based on "age-wise distribution", 1-5 years were found to be 103 (57%), 6-10 years were 54 (30%), 11-14 years were 24 (13%).

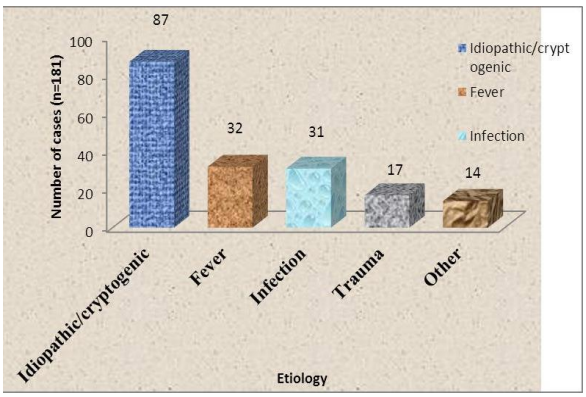


Fig 03: Various Etiologies Observed From this chart it is evident that

The most common etiology observed is idiopathic/cryptogenic cause followed by fever.

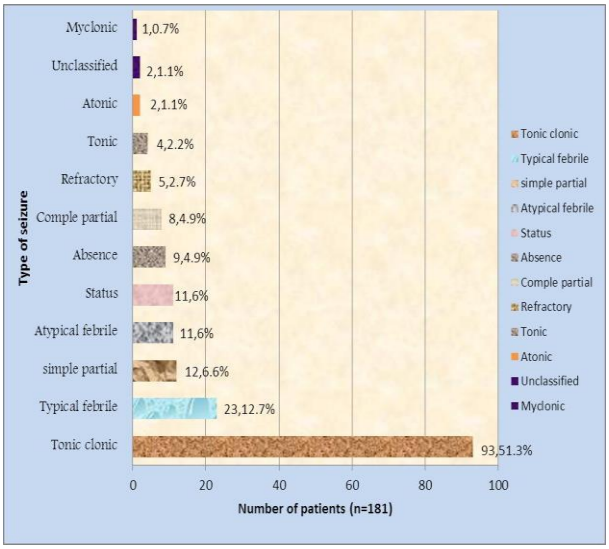


Fig 04: Distribution of Study Population-Based On the Type of Seizure

From this chart, it is evident that tonic-clonic seizures are the most commonly seen seizure type in children followed by febrile seizures, and rarely seen is myoclonic seizures.

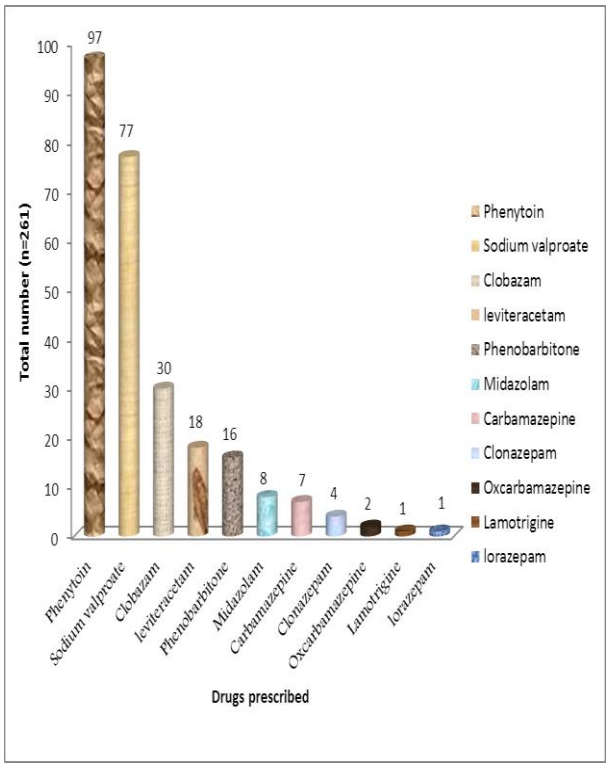


Fig 05: Anti-Epileptic Drug Distribution

From this chart it was found that phenytoin, sodium valproate and clobazam were commonly prescribed AED's in children. The least prescribed drug is lamotrigine and lorazepam. Irrespective of type of seizure, Diazepam is commonly prescribed drug for the emergency management of seizures.

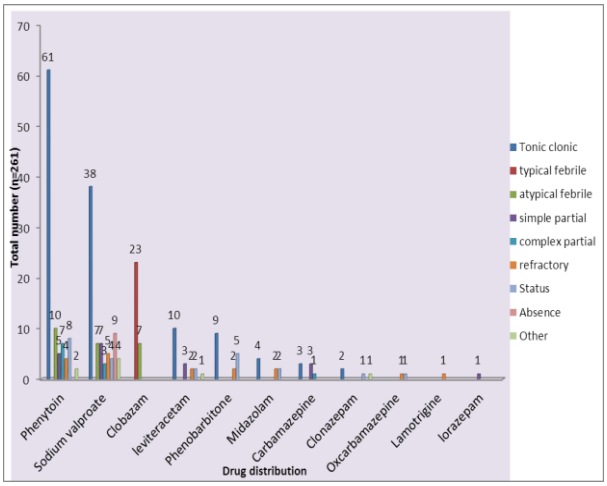


Fig 06: Distribution of Drugs In Relation To Seizure Type

From this chart, it is found that fortonic-clonic seizures, phenytoin is commonly prescribed followed by sodium valproate, levetiracetam, and phenobarbitone is given alone or in combination with other drugs. For typical febrile seizures, the only drug prescribed is clobazam. For simple partial seizures valproate is the most commonly prescribed AED and for complex phenytoin is commonly prescribed. For refractory seizures, a multiple drug regimen is preferred among which the broad spectrum AED valproate followed by phenytoin are most common.

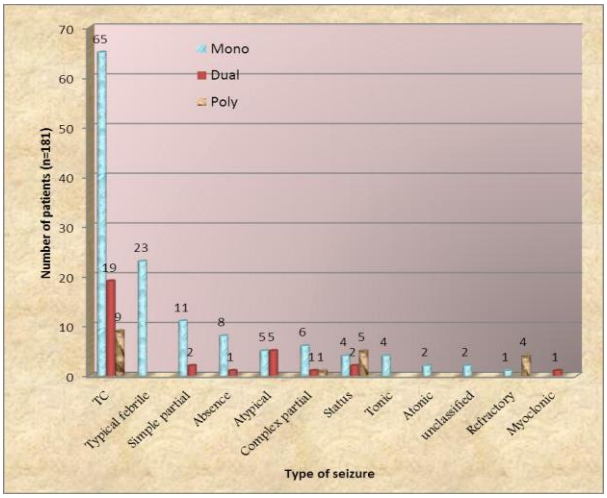


Fig 07: Choice of Therapy for Different Types of Seizure

From this table it was found that out of 181 patients, 131 (72%) were on monotherapy and 50 (28%) were on Combination therapy of which 31 (17%) were on dual therapy, 19 (11%) were on polytherapy ( >2 AED's). It was found that monotherapy is commonly preferred for

Tonic clonic seizures 65 (69%) followed by febrile seizures. Combination therapy was preferred commonly for tonic clonic seizures followed by Status epilepticus.

Table 01: Change in Drug Therapy

| Initial drug | Changed to | Total number of patients (n= 16) |
|---|---|---|
| Phenytoin | Sodium valproate | 11 |
| Carbamazepine | Sodium valproate | 3 |
| Carbamazepine, Phenytoin | Sodium valproate | 2 |

Out Of 16 patients in whom the drug therapy has been changed, the Sodium valproate has been the drug of choice irrespective of the prior therapy (Phenytoin, Carbamazepine). The broad-spectrum AED, Sodium valproate has been selected as it was found to be more efficacious than other drugs that are given to achieve the required therapeutic outcome.

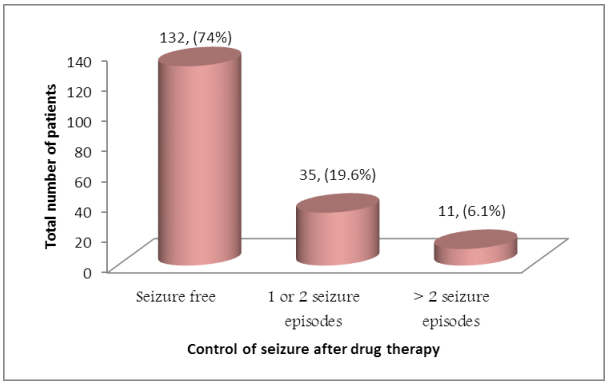


Fig 08: Efficacy of Drug Therapy

Among the 181 in-patients who have come for follow up to Pediatric OP are considered as the study of interest among which 3 were found to be dead because of other co-morbid conditions and in the remaining 178 patients-
patients with Seizure free period - 132 (74.14%)
patients with 1-2 seizure episodes of seizures - 35 (19.66%)
patients with >2 seizure episodes seizures - 11 (6.17)

**Observed Adverse Drug Reaction**

The incidence of ADRs in the considered study group is less (i.e, 6.6%) and is observed only in 12 patients. A combination of ADRs were also observed in few patients (5 patients developed 3 ADRs each and 2 patients developed 2 ADRs each). ADRs due to Phenytoin were observed in greater number of patients i.e. 6 (Ataxia, letheragy, Gum hypertropy, Rash, leukopenia, and Reactive lymphadenopathy) of which one has developed Phenytoin toxicity. ADRs due to Sodium valproate was observed in 5 patients (Jaundice, rash, hematological-related ADR thrombocytopenia). Carbamazepine-induced hepatotoxicity was experienced by one patient. As the ADRs incidence is low with the regimen given the required outcome has not been altered.

## Discussion

The total number of subjects included in this non-experimental prospective observational study conducted for 6 months duration between march 1st to august 31st is 181 among which a number of female patients is greater than male patients. There is a significant difference in gender variation found in many studies but the reason behind this is not well established. As found in many other studies, the prevalence of seizures is observed to be high among age group 1-5years and low among 11-14 years. Types of seizures observed are tonic-clonic (51.3%), Typical febrile seizures (12.7%). According to guidelines and other studies tonic-clonic seizures are the most common type. Based on etiology, a number of cases with idiopathic/cryptogenic causes are more followed by fever, infection, trauma, and others, which varies from study to study. The most prescribed drug in our study is phenytoin which varies from other south Indian studies, where it was underutilized, in spite of being less expensive. Phenytoin was also the most frequently prescribed drug in some studies conducted in India on drug utilization patterns. According to studies in India and other countries, phenytoin is a mostly prescribed drug followed by valproic acid. Monotherapy is observed in 72% of patients which is evident in many studies and combination therapy is observed in 28% of patients among which dual therapy is seen in 17% patients and polytherapy in 11% patients. Other studies also document the preference of single drug approach since polytherapy exposes the patients to unnecessary hazards like drug allergy, drug interactions, noncompliance, and economic burden. Of 16 patients in whom the drug therapy has been changed, the Sodium valproate has been the drug of choice irrespective of the prior therapy (Phenytoin, Carbamazepine). Sodium valproate has been selected as it was found to be more efficacious than other AED's that are given to achieve required therapeutic outcome. Outcome of the therapy is measured by seizure free period which is estimated by follow-up in OPD and by contacting them through

phone calls, among which 74.1% are observed seizure free, 19.66 are observed with 1-2 episodes of seizures and 6.1% are observed with more than 2 episodes. The incidence of ADRs in the considered study group is less and is observed only in 12 patients (6.6%) and the drug with more ADRs seen is phenytoin followed by sodium valproate, which is evident in many other studies. ADRs observed are ataxia, gum hypertrophy, lethargy, reactive lymphadenopathy, rash, jaundice, hepato-toxicity. Medication adherence is measured in known epileptic patients (n=67) using MMAS (Morisky's medication adherence scale) among which 31% are highly adherent, 49% are medium adherent and 13% are low adherent. Here, patients with medium adherence seems to be more and the reason behind it was found to be low socioeconomic status, lack of awareness on significance of compliance.

## Conclusion

In this study, we observed prevalence of seizures among age group 1-5years to be high and mostly seen type of seizure is tonic-clonic. Highly distributed and prescribed drug in this teritiary care hospital is phenytoin and most of the ADR's seen are due to this drug followed by valproic acid. ADR's observed are very less. Monotherapy is mostly seen and found efficacious with good compliance, hence it is preferred and recommended. Irrespective of type of therapy i.e. monotherapy or combination therapy monitoring is required to prevent ADR's. In some patients, due to lack of desired outcome with prescribed anti-epileptic, it is replaced with broad-spectrum anti-epileptic, sodium valproate, which is found effective. By using Morisky's medication adherence scale, it is found that patients with medium adherence are more. Taking considerable follow-ups it is observed that patients with seizure free are more than patients with 1-2 episodes and more than 2 episodes of seizures, therefore treatment given is found effective. By explaining and counselling about the importance of adherence to medication, treatment outcome was found effective. Clinical pharmacist has a pivot role in conducting drug utilization studies that helps in comparing the ongoing regimen with the standard treatment guidelines so as to promote the stupendousity of rational use of drugs and to minimize or control the incidence of ADRs. The study can be made more reliable by conducting long term studies.

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