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Research Article

# STUDY OF USAGE PATTERN AND SIDE EFFECTS TO ANTI-EPILEPTIC DRUGS IN PEDIATRIC PATIENTS

**Mounika M[1*]., Tejaswini M[1]., Raju M.S[2] and RamaRao N.V[1]**

[1]Department of pharmacy practice, Chalapathi Institute of Pharmaceutical Sciences, Guntur
[2]Department of Pediatrics, Government General Hospital, Guntur

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**ABSTRACT**

**Background:** Worldwide, up to 80 million people are suffering with epilepsy, of whom 10.5 million are children <15 years. The lifetime likelihood of experiencing at least 1 epileptic seizure is about 9%. Because of common occurrence of epilepsy, the narrow therapeutic index and safety margins of antiepileptic medications, and the recognized side effects of medications, in children with epilepsy is imperative. This study reviews the usage pattern and side effects to the anti-epileptics in children. Appropriate usage pattern of antiepileptic drugs in childhood epilepsy is essential to improve quality of life in these children.

**Aim:** To study the pattern of usage and side effects to anti-epileptic drugs in pediatric patients.

**Objectives:**

1. To study the prescribing pattern of anti epileptic drugs
2. To identify the side effects experienced by the pediatric patients

**Methodology:** The study was conducted in Government General Hospital, Guntur, a tertiary care teaching hospital. The sources of data included were relevant medical records of the patient along with direct observation of the patient. Socio-demographics of the patient, anti-epileptic drugs prescribing pattern, associated drug related problems and adherence were considered during the process of data collection.

**Results:** During the study period, 148 subjects of either sex were enrolled. In this 34 of the 148 children (22.9 %) were on multiple AED; 31(20.9) were on dual therapy while 3(2%) were on triple therapy. The most common drug combination was Valproic acid (VPA) and Phenytoin (PHT) followed by VPA and Clobazam.

**Conclusion:** Sodium valproate was the most commonly prescribed drug. Major side effects reported were with sodium valproate (somnolence, weight gain, nocturnal enuresis.)



## INTRODUCTION

Epilepsy is a disease of the brain defined by any of the following conditions

1. A least two unprovoked (or reflex) seizures occurring >24 h apart
2. One unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next 10 years
3. Diagnosis of an epilepsy syndrome

Epilepsy is considered to be resolved for individuals who had an age-dependent epilepsy syndrome but are now past the applicable age or those who have remained seizure-free for the last 10 years, with no seizure medicines for the last 5 years. (1)

**Corresponding author:* **Mounika M**
Department of pharmacy practice, Chalapathi Institute of Pharmaceutical Sciences, Guntur

Epilepsies affect at least 2% of the population at some time in life, and many forms have genetic determinants I, II. We have found a mutation in a gene encoding a GABA-A receptor subunit in a large family with epilepsy.(2,3) The two main phenotypes were childhood absence epilepsy (CAE) and febrile seizures (FS). There is a recognized genetic relationship between FS and CAE, yet the two syndromes have different ages of onset, and the physiology of absences and convulsions is distinct. (3)

The management of epilepsy in children requires careful evaluation, classification, and pharmacologic treatment (4,5). With classic antiepileptic drugs (AEDs), at least 25% of children remain refractory to appropriate therapy. The past decade has allowed the introduction of a number of newer AEDs for treatment of both adults and children with epilepsy. These include Felbamate, Gabapentin, Lamotrigine, Topiramate, Tiagabine, and Vigabatrin. Emerging information regarding the efficacy of these AEDs in treating childhood

epilepsy syndromes suggests advantages for many patients[4,5]. Limited data are available that define the optimal use of new AEDs in pediatric patients. Further research must be completed to validate the positive effects described in existing clinical trials of the new AEDs in the treatment of childhood epilepsy.[6]

The decision to treat a child with a drug depends upon the individual (frequency of seizures, epilepsy syndrome and neurological findings). It remains unclear when drug treatment should begin, and numerous attempts have been made to accurately predict the risk of epilepsy developing (i.e. recurrent, spontaneous seizures).[7] Most clinicians would not recommend starting treatment after a single, brief generalized tonic-clonic seizure, but would after a cluster of seizures or, possibly, after an episode of unprovoked status epilepticus. Similarly a child with severe physical and learning difficulties who develops infrequent myoclonic or generalized atypical absence or focal seizures may not necessarily require an AED. [8]

Seizure medicines may cause unwanted side effects in some people. Most of the time, the effects are mild and don't last long. Often they can be treated by adjusting the dose or how a person takes it.[9]

Children with epilepsy are at increased risk of side effects. Use of oral Clobazam or Diazepam for 2 days may be beneficial in decreasing this risk. A child who is brought to the physician from an extramural setting still convulsing should be considered to be in side effect; the minimum time for this definition of side effect is regarded as >5 minutes. There is an increased risk of irreversible neuronal injury after 30 minutes of convulsive status. [10]

## METHODS AND METHODOLOGY

***Study Design:*** Prospective Observational Study

***Study Period:*** The study was conducted in a period of 6 months i.e., from December 2016 to May 2017.

***Study Method:*** The study was conducted in Government General Hospital, Guntur, a tertiary care teaching hospital. The data was obtained from direct observation of the patient and the information received by the patient caregivers during follow up. Socio-demographics of the patient, anti-epileptic drugs prescribing pattern, associated drug related problems were considered during the process of data collection.

***Materials Used***

- Informed consent form (by the caregivers)
- Case report form
- Patient counseling form and information leaflets.

***Inclusion criteria***

- Patients with epilepsy between age group of 1-12 years.
- Who were on anti epileptics from more than 1 month
- Who had data on the presence or absence of parental consanguinity

***Exclusion Criteria***

- Above 12 years of age, below 1 year of age
- Who were on anti epileptics for less than 1 month
- Whose parents or guardian had not authorized their participation in the study

## RESULTS

**Table 1** Age and Gender wise distribution

| Age group | Male children | % | Female children | % |
|---|---|---|---|---|
| 1-4yrs | 14 | 9.4 | 24 | 16 |
| 5-8yrs | 31 | 20 | 27 | 18 |
| 9-12yrs | 33 | 22.2 | 19 | 12.8 |

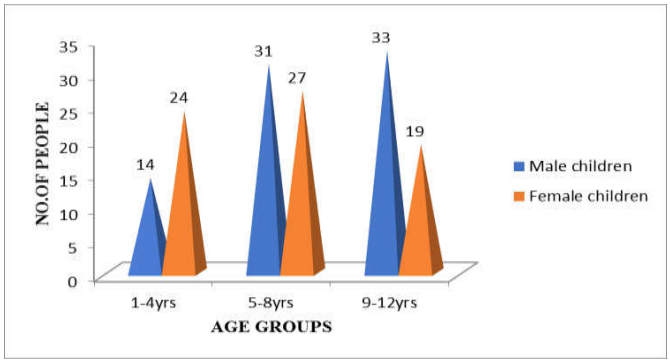


**Figure 1** Age and Gender wise distribution

Figure 1 represents gender wise distribution of seizure disorder and was found to be more in male children of age group 9-12 yrs when compared to 1-4yrs and 5-8 yrs respectively. Overall male children are more prone to seizures than female children in this study population

**Table 2** Type of Therapy

| Category | Monotherapy | No of patients (114) |
|---|---|---|
| Iminostilbene | CBZ | 4 |
| Benzodiazepine | CLB | 5 |
| Newer drug | LEV | 2 |
| Barbiturates | PB | 2 |
| Hydantoin | PHT | 26 |
| Alpha carboxylic acid | VPA | 75 |
| | **Polytherapy** | **No of patients (34)** |
| | VPA,PHT | 15 |
| | VPA, LEV | 4 |
| | VPA,CBZ | 2 |
| | VPA,CLB | 6 |
| | VPA.CLB,LEV | 1 |
| | VPA,PHT,LEV | 2 |
| | PHT,CBZ | 1 |
| | PHT,LEV | 1 |
| | PHT,CLB | 1 |
| | CLB,LEV | 1 |

Table 2 represents single and multiple antiepileptic use of drugs in the study sample. In this 34 of the 148 children (22.9 %) were on multiple AED; 31 were on dual therapy while 3 were on triple therapy. The most common drug combination was VPA and PHT, 15/34 (44.1 %) followed by VPA and CLB, 6/34(17.6%). Of the 114/148 participants on monotherapy, 75/148 (50.6 %) were on VPA only, and 28/148 (18.9 %) were on PHT only, five were on CLB only, 4 were on CBZ and 2 were on LEV and PB each

**Table 3** Rationalization of monotherapy

| Seizure type | No of patients using monotherapy | 1st line | 2nd line | Alternative |
|---|---|---|---|---|
| Absence | 2 | 2 | 0 | 0 |
| Atonic | 5 | 5 | 0 | 0 |
| Atypical Febrile | 17 | 5 | 8 | 4 |
| Clonic | 1 | 1 | 0 | 0 |
| Complex partial | 13 | 0 | 13 | 0 |

| | | | | |
|---|---|---|---|---|
| Focal | 4 | 4 | 0 | 0 |
| GTCS | 56 | 37 | 1 | 18 |
| Infantile spasm | 1 | 1 | 0 | 0 |
| Myoclonic | 4 | 4 | 0 | 0 |
| Tonic | 11 | 5 | 0 | 6 |

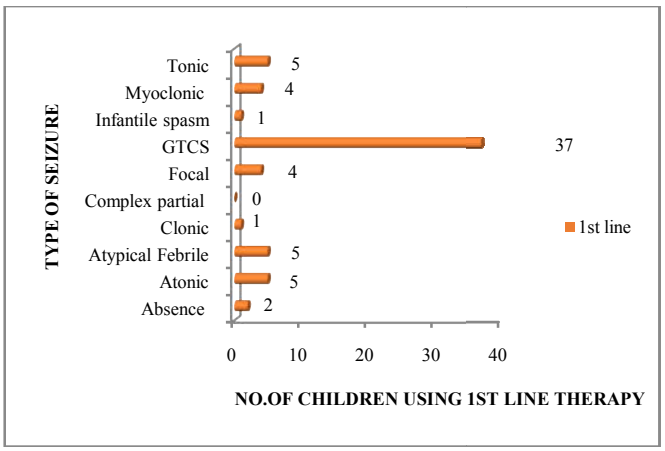


**Figure 2** No of children using 1st line therapy

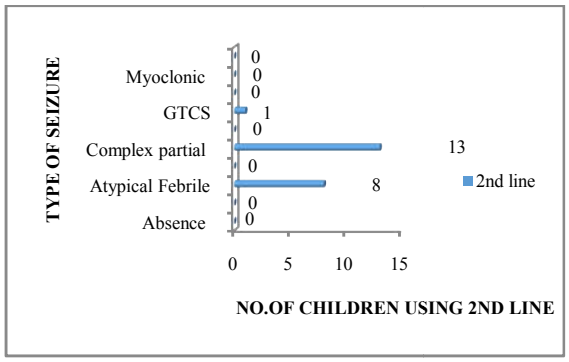


**Figure 3** No of children using 2nd line therapy

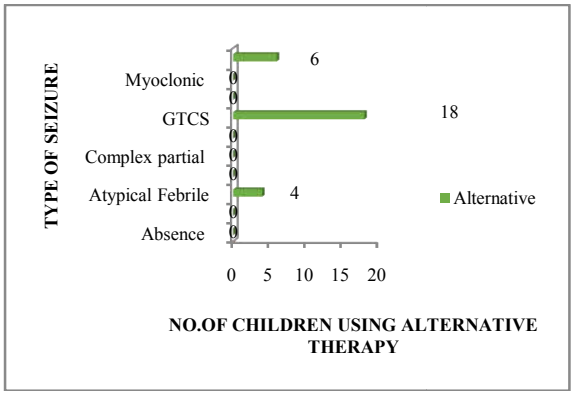


**Figure 4** No of children using alternative therapy

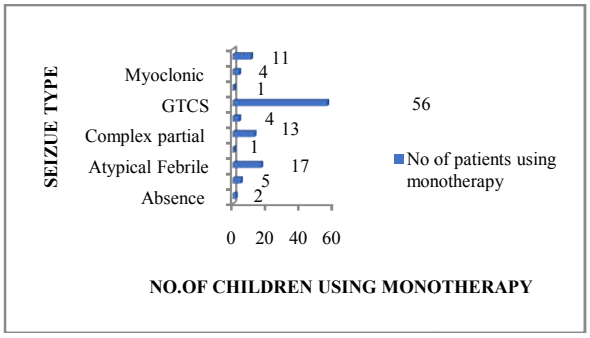


**Figure 5** No of children with monotherapy

Table 3 depicts the rationalization of monotherapy among the children using anti-epileptic drugs. Most of the children are receiving rational therapy n=86(75.4%) of them 64 children are receiving 1st line therapy and 22 are receiving 2nd line therapy.

**Table 4** No of rational and irrational prescriptions in monotherapy

| Rational prescriptions | Irrational prescriptions |
|---|---|
| 86 | 28 |

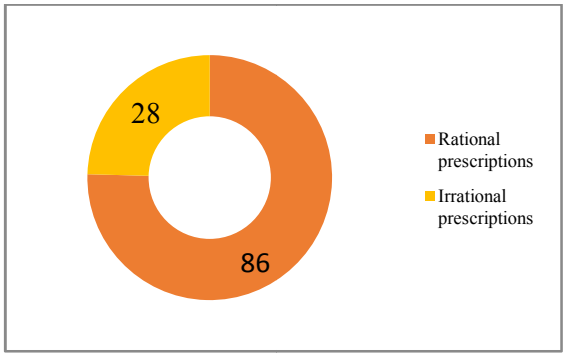


**Figure 6** No of rational and irrational prescriptions in monotherapy

**Table 5** Side effects associated with antiepileptic drugs

| Drug | Side effect | No of patients |
|---|---|---|
| Sodium valproate | Somnolence | 3 |
| | Weight gain | 5 |
| | Nocturnal enuresis | 1 |
| Clobazam | Constipation | 1 |
| Phenytoin | Gingival hyperplasia | 1 |

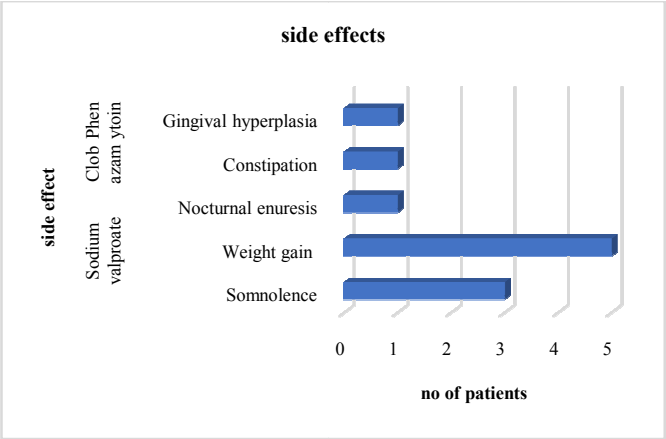


**Figure 7** Side effects associated with antiepileptic drugs

Table 5 depicts side effects associated with antiepileptic drugs. Out of 148 sample size 11 side effects are reported. Nearly 81% of the side effects were due to Sodium valproate following 19% each with Clobazam and Phenytoin.

## DISCUSSION

A prospective observational study on usage pattern and side effects of anti-epileptic drugs was conducted in paediatric population in the age group of 1-12 years in tertiary care hospital for a duration of 6 months. During the study period the data was collected tabulated & analysed. On reviewing the demographic data, it was found that age has a major impact on incidence of seizures. In our study we found that majority (n=110, 74.3%; In Fig:1) of patient who were suffering from seizures are in between the age group of 5-12yrs old and were males. This result was in concordance with the study done by Siddhartha kiran Gollapalli *et al.*, which showed that seizure

disorders were mostly experienced in the age group of 3-10 years and were more common in males.

With regards to various types of seizures our study showed that Generalised seizures (50%) has a major incidence. In Generalised seizures greater percentage (78.1%) of patients were diagnosed with generalised tonic clonic seizures and in partial seizures 90% of the children are with complex partial seizures. These results were in concordance with the study conducted by Siddhartha kiran Gollapalli *et al*. [11,12] , which stated that there was a higher incidence of generalized seizures (55.56%) compared to partial seizures (32.40%). Generalised tonic clonic seizures (91.67%.), Complex partial seizures (82.86%) were the commonest type of seizures among Generalized and partial seizures respectively.

Generally, Antiepileptic drug (AED) monotherapy is the preferred initial management approach in epilepsy care, since most patients may be successfully managed with the first or second monotherapy. In our study majority were on monotherapy about (n=144, 77%) of the subject population among which (n=86,75%) of the monotherapy prescriptions are considered as rational. Among Monotherapy Sodium valproate (50%) was considered as preferred treatment. This study was similar to the study done by Erik K. St. Louis *et al*. [13] Based on our findings Polytherapy is preferred in patients with recurrent seizures or the children who had a family history intolerable to anti-epileptic drugs. Among polytherapy most of the patients were receiving dual AED and most common drug combination was found to be VPA and PHT (n=32, 38.2 %) followed by VPA and CLB (17.6%).

In our current study we also observed the side effects commonly associated with antiepileptic drugs. Among them somnolence, weight gain, nocturnal enuresis are associated with valproate (n=9, 81%; Fig: 4)

## CONCLUSION

Based on our current prospective observational study we concluded that male children were predominant than the female children. Generalized tonic clonic seizures was the most common type among various types of seizures. Monotherapy is preferred regimen and the Sodium valproate is the widely used drug among other AED. As sodium valproate is the most commonly used drug most of the side effects reported with it are somnolence, weight gain, nocturnal enuresis. Gingival hyperplasia and constipation are other side effects reported with Phenytoin and Clobazam respectively.

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