



## Study on anti-epileptic drugs used in children to treat various types of epilepsy in tertiary care hospital

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### Abstract

**Aim:** This study was aimed to study about anti epileptic's drugs utilization pattern and cost effective analysis among children in tertiary care hospital.

**Materials and methods:** In this observational study 71 patients were enrolled from inpatient and outpatient of Pediatrics Department in RMMCH during the study period i.e., from November 2016 to April 2017. Morisky scale, statistical analysis-paired t test were used to assess medication adherence and cost effectiveness respectively. Resources used for the collection of the data include, Patient case sheet and Personal interaction with the patients.

**Results:** The study showed that epilepsy attacks were found to be more common in male (73.24%) than female (26.76%) patients. In this study, majority of patients were on monotherapy (56.3%) and less were on triple therapy (8.45%). Valproate are prescribed more (17.5%) followed by Phenytoin (15%). Medication adherence was improved after patient counseling.

**Conclusion:** The periodic studies on drug utilization pattern of antiepileptics would help in understanding the trends of use in comparison with other reports or facilities and also that more involvement of pharmacist in children care yields better therapeutic outcomes. As our study is the first of its kind this serves as baseline data for future reference.

**Keywords:** antiepileptics, drug utilization

### Introduction

Epilepsy is a disorder of the central nervous system characterized by periodic loss of consciousness with or without convulsions associated with abnormal electrical activity in the brain. In some cases it is due to brain damage, but in most cases the cause is unknown. (Suruchi Sharma, et.al 2013) Epilepsy is a common, sometimes chronic, neurological condition with physical risks and psychological and socioeconomic consequences which impair quality of life. It is estimated that there are more than 10 million in India and more than 50 million people with epilepsy worldwide. Epilepsy foundation has also estimated that every 1 in 26 people in United States of America will develop epilepsy at some points in their life time.

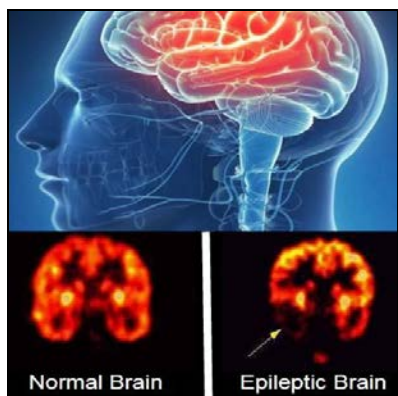


Fig 1

Epilepsy is one of the most common of the serious neurological disorders. (Chandi Charan Kandar, et.al 2012) It is estimated that there are 55 lacks persons with epilepsy in India, 20lacks in USA and 3lacks in UK. Each year 120 per 100,000 people in the United States come to medical attention because of a newly recognized seizure. At least 8% of the general population will have at least one seizure and not have epilepsy. The rate of recurrence of a first unprovoked seizure within 5 years Ranges between 23% and 80%.6 the age adjusted incidence of epilepsy is 44 per 100,000 people in a year. Each year about 125,000 new epilepsy cases occur; of these, 30 % are in people younger than age 18 at the time of diagnosis. The relatively high frequency of epilepsy in the elderly is now being recognized. At Least 10 % of patients in long- term care facilities are taking at least one antiepileptic drug (AED).

The National Sentinel Audit of Epilepsy-Related Deaths led by 'Epilepsy Bereaved' drew attention to this important problem. The Audit revealed; "1,000 deaths occur every year in the U.K. as a result of epilepsy" and most of them are associated with seizure and 42% of deaths were potentially avoidable.

### Aim of the Study

The primary source of the study was to evaluate the drug use pattern, cost-effectiveness, medication adherence and seizure outcome of newer and older antiepileptic drugs in pediatric clinical practice in an Indian hospital setting (Rajah Muthiah Medical College and Hospital (RMMCH), Annamalai Nagar-608002, Tamilnadu).

### Epidemiology

## Seizures Classification

International classification of epileptic seizures proposed by the Commission on Classification and Terminology of the International League against Epilepsy (ILAE) and approved in September 2013. (Suruchi Sharma, Vaishali Dixit 2013) This classification is based on the clinical expression of the seizure and the electroencephalographic picture during and between the seizures.

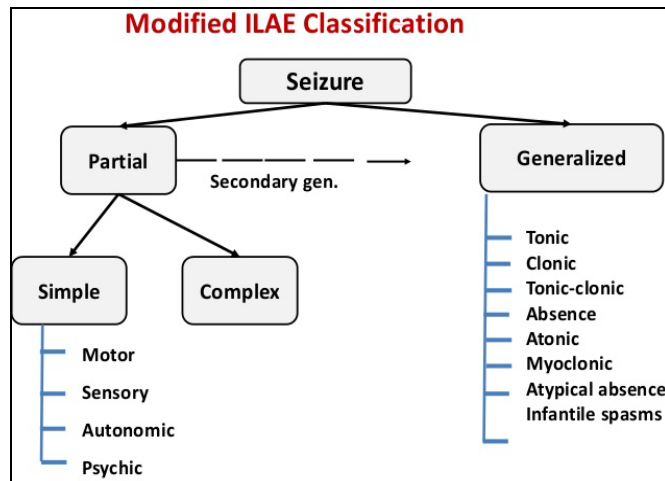


Fig 2

## Management of epilepsy

The terms anticonvulsant and antiepileptic are used interchangeably. An anticonvulsant is an agent that blocks experimentally produced seizures in laboratory animals and antiepileptic drug is a drug used medically to control the epilepsies.

### Principles of management

1. Any causative factors of epilepsy must be treated, e.g. cerebral neoplasm.
2. The patients should be educated about the disease, duration of treatment and need for compliance.
3. Precipitating factors should be avoided, e.g. alcohol, sleep deprivation, emotional stress.
4. Natural variation should be anticipated, e.g. fits may occur particularly or exclusively around periods in women.
5. Antiepileptic drug should be given only if seizure type and frequency require it, i.e. more than one fit every 6-12 months.

### Objectives

- To study the socio demographic characteristics of epilepsy patients.
- To study the drug use pattern in pediatrics epilepsy.
- To find out medication adherence in children with epilepsy.
- To study cost effective analysis of anti-epileptic drugs.

## Methods

The study was conducted in Ward and out patients of Department of pediatrics, Rajah Muthiah Medical College Hospital, Annamalai University, Annamalai Nagar, Chidambaram, Tamil Nadu, which is 1400 bedded multi-specialty tertiary care teaching hospital located in rural South India. The study was approved by the Institutional Human Ethics Committee & Informed Consent Form was obtained from the eligible patients and a total of 71 partruients were selected on the basis of inclusion criteria and exclusion criteria.

### Inclusion criteria

- Patients admitted in pediatrics ward and outpatient diagnosed with seizures.
- Patients who are the age group of 1 month to 12 years.
- Patients whose parents are complies to give consent.
- Patients whose past history is needed to require.

### Exclusion criteria

- Patients whose parents are not willing to participate.
- Patients who lost follow up.

### Sources of data

The data will be collected from the patients admitted for fine confinement in labour ward of obstetrics & gynaecology of RMMCH. The various sources used for collection of data include:

- Patients case sheets maintained in the hospital.
- Patient interview.

### Assessing of prescribing pattern

In the present study the prescribing pattern was conducted to evaluate to drug-prescribing trend of anti-epileptic drugs by physicians in RMMCH. In this study the categories of drugs, drug therapy regimens, list of drugs complying with WHO, NATIONAL, T.N EDL was analyzed by including the number of prescriptions. Finally all the 71 patients' prescriptions were analyzed and a result was tabulated according to their percentages and number of prescriptions.

### Assessing medication adherence

The data collection tool used was a questionnaire consisting of the Morisky self-reported medication adherence questions related to medication (Morisky *et al*, 1989). The morisky self-reported medication adherence scale/score is a commonly used adherence screening tool. It is composed of 7 –yes/no questions about past medication use patterns and thus quick and simple to use during drug history interviews. In the Morisky scale, a NO answer was allotted a score of 0, and a YES a score of 1. By using this medication adherence scale improvement of adherence towards medication will be measured as LOW, MEDIUM, and HIGH adherence.

### Assessment of cost effectiveness

It was calculated as ratio of cost of treatment and improvement in quality of life with every combination. The direct medication cost was calculated in Indian national rupees

(INR). Retail price of each drug as per Indian drug regulation in current time was recorded. Statistical analysis: Statistical analysis was done using paired “t test” for intra-group comparison. The value of  $p < 0.05$  was considered statistically significant.

**Statistical analysis**

The statistical test used for analyzing collected data results was done by using Mann-Whitney U test is the non-parametric alternative test to the independent sample t test. It is a non-parametric test that is used to compare two sample means that come from the same population, and used to test whether two sample means are equal or not. Usually, the Mann-Whitney U test is used when the data is ordinal or when the assumptions of the t-test are not met.

The incremental cost-effectiveness ratio (ICER) is a statistic used in cost-effectiveness analysis to summarize the cost-effectiveness of a health care intervention. It is defined by the difference in cost between two possible interventions, divided by the difference in their effect.

**Results and discussion**

The study described the prescribing pattern, medication adherence, cost effective analysis of epilepsy patients in a 71 pediatrics patients observed and followed up in a tertiary care hospital for duration of six months. Total of 71 patients were enrolled using inclusion criteria and exclusion criteria.

**Demographic Data**

**Table 1:** Age Wise Distribution

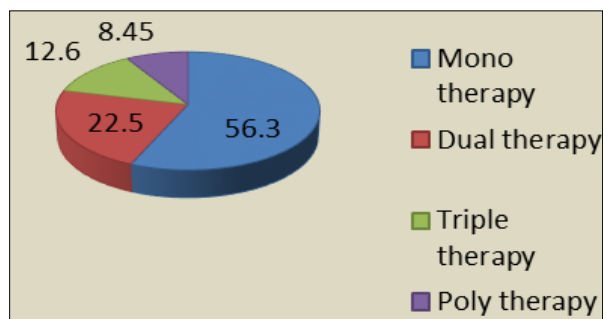
Age Groups (Years)	No. of Patients	Percentage (%)
0-03	28	39.4
03-05	23	32.4
05-09	17	23.9
09-12	03	04.2

Below table represents the age wise distribution of patients participated in the study. Child was divided into 4 groups. < 3 years, 3-5 years, 5-9 years, 9-12 years.

**Gender Wise Distribution**

Almost 39.4% were in the age group of < 3 years and 32.4% were in the age

Group of 3-5 years. Rests around 28.1% were in 5-12 years age group.



**Fig1:** Therapy Wise Distribution

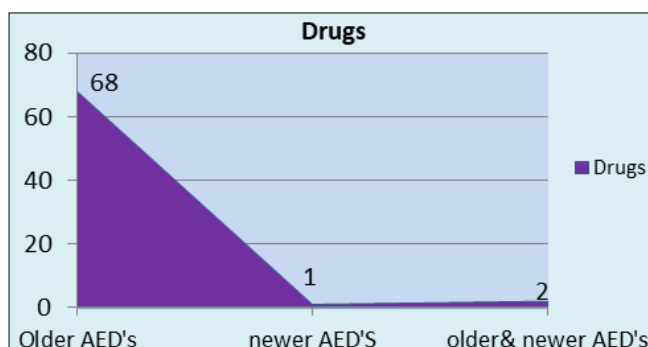


**Fig 2:** Gender Wise Distribution

Almost 73.24% were male patients and 26.76% were female patients. This was in accordance with the study done by k. bhanupriya and a. dulcie celia (2015) in Pediatric neurology department, Tirunelveli Medical College Hospital, Tirunelveli of which Male (64%) are predominance of Female (44%).

**Fig 3: Drug Therapy**

In our study majority (56.3%) of patients were on Monotherapy, (22.5%) on dual therapy, (12.6%) on triple therapy and (8.45%) on Polytherapy which is in accordance with the study by maity N and niveditha gangadhar (2013) evaluated the AED utilization pattern in pediatric clinical practice in a tertiary care hospital setting, majority (63.8%) of patients were on Monotherapy and 36.2% on dual, triple and Polytherapy



**Fig 3:** older and newer aed's

Valproate (17.5%) was the commonly prescribed drug followed by phenytoin (15%). This was in contrast to a community based study in UK where there was slight preponderance of Valproate (22%) followed by Carbamazepine (21.3%) as most commonly used AED.

**Table 2:** Medication Adherence

Group	N	Median	25%	75%
Control	71	2.000	2.000	4.000
Test	71	2.000	1.000	3.000

Mann-Whitney U Statistic= 1693.00

T = 5904.00

P = <0.001

The difference in the median values between the two groups is greater than would be expected by chance; there is a statistically significant difference ( $p = 0.001$ )

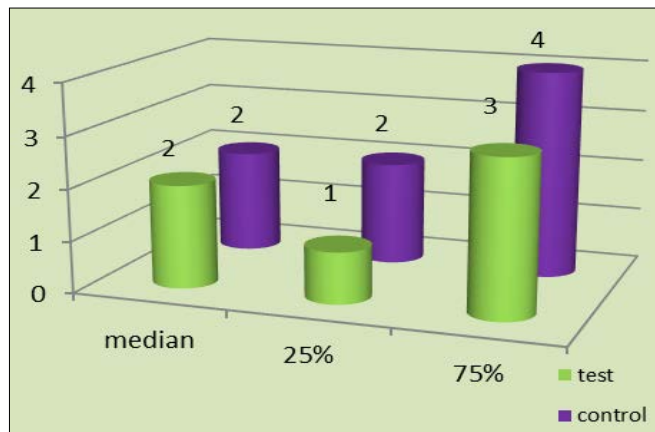


Fig 4: Medication Adherence

Adherence to the prescribed medication plan is crucial in pediatric patient with epilepsy to be seizure free. When comparing follow up 1 (control) and follow up 2 (test) the difference in the median values between the two groups is greater than would be expected by chance; there is a statistically significant difference ( $p = 0.001$ ) and it shows increase in adherence in test results our results are also consistent with the study conducted by hommel and baldassano (2009) and logan et-al (2003) indicated a non-adherence % to anti-epileptic medication by 75%

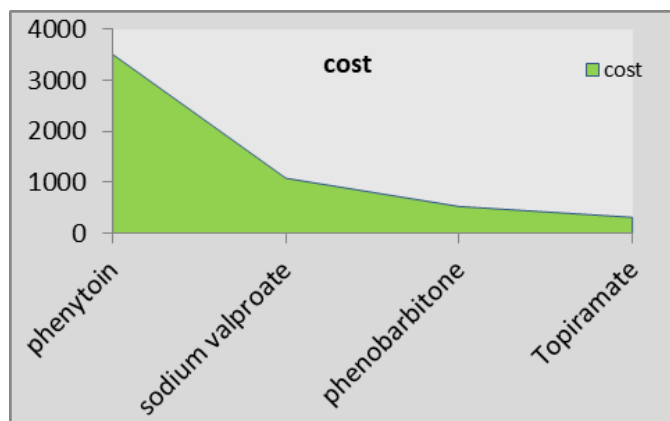


Fig 5: Cost Effectiveness of Aed's:

Incremental cost effective ratio of individual drugs (old AED's compared to newer AED'S)

ICER For phenytoin relative to topiramate:

- Total cost spent on phenytoin = 3507.5
- Total seizure free patients = 17
- Cost involved to produced single  
= Rs (3507.5/17)  
= Rs 206.32
- Cost involved to produced single with topiramate = 312  
ICER = 312-206.32/1  
=105.68 Rs
- ICER for valproic acid relative to topiramate  
ICER = 312-107.76  
= 204.24 Rs
- ICER for phenobarbitone relative to topiramate  
ICER = 312-52.38  
= 259.62 Rs

On finding ICER of individual drugs (comparing old and new AED) more cost was spent on phenobarbitone & topiramate (259.6 Rs) followed by valproic acid (204.24 Rs).

### Summary

- For the acute management of seizures, monotherapy was found to be the most preferred choice of treatment and in this, valproate was the preferred drug of choice.
- Most of the treatment strategies are adopted from WHO guidelines and WHO EDL.
- Patient education increased the knowledge about epilepsy and importance of self-care, and life style modifications that can lead to better control of the disease among the patients. By the end of the study there was a significant increase in the medication adherence score.
- At base line all patients had poor knowledge and attitude towards their disease. At the end of the study patients of interventional group received extensive education regarding their disease and its management showed greater improvement in treatment outcomes than in patients in control group.
- Adherence to the prescribed medication plan is crucial in pediatric patients with epilepsy to be seizure free.
- Medication adherence results suggest that more involvement of pharmacist in patient care yields better therapeutic outcomes.
- Parents need more supportive and explore different ways to increase the adherence by using different methods like medication organizer or alarm.
- Pharmacist holds an important role in educating the patient about disease thereby avoiding the trigger factors and reducing the hospitalizations.
- In conclusion, patient counseling aided and had a positive impact on patient's understanding of their illness and the role of medications in its treatment, improved medication adherence. Moreover, a good professional rapport has been built between the pharmacist and the patient.

### Conclusion

Our study showed that male is more affected with epilepsy than female. Patient of age groups of < 3 years, 3-5 years more affected than other age groups. Valproate is the most commonly prescribed drugs for epilepsy followed by phenytoin. A medication adherence result was increased after patient counseling. Suggest that more involvement of pharmacist in patient care yields better therapeutic outcomes. In comparison of new and old AED the incremental cost effectiveness ratio was high for phenobarbitone followed by valproic acid.

### Limitation of the Study

The number of patients obtained and the study duration were limited. If the study was conducted for longer duration, more significant.

The study was single centered with small sample size and done only in pediatric age group. Recommends multi centric study in general population.

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