



RESEARCH ARTICLE

Drug Utilization Pattern of Antiepileptic Drugs and Adverse Effects in Paediatric Unit of a Tertiary Care Teaching Hospital

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Conflicts of Interest: Nil

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ABSTRACT

To study drug utilization pattern of antiepileptic drugs and their adverse effects in paediatric department in a tertiary care teaching hospital. **METHODOLOGY:** A prospective interventional study was done on patients admitted in paediatric department of Maharaja Institute of Medical Sciences, Vizianagaram, Andhra Pradesh, India. Information regarding age, gender, types of AEDS prescribed and adverse effects, episodes of seizures were recorded in a standard questionnaire (case report form). **RESULTS:** Total of 100 seizure cases were included after excluding missing data. Out of 100 cases, 67 were male and 33 were female, below 5 years 33 cases, 5-10 years 30 cases, 10-15 years 22 cases and 15-18 years 15 cases were collected. **CONCLUSION:** based on data collected seizures, which occurred mostly in the male between the age groups of 0-5 years compared to females.

Keywords: phenytoin, epilepsy, seizures

Introduction

EPILEPSY:

According to the World Health Organization, "epilepsy refers to a group of chronic brain conditions characterized by recurrent epileptic seizures". These seizures are the clinical manifestations of excessive and/or hyper-synchronous, usually self-limited, abnormal activity of neurons in the brain.

ETIOLOGY:

Seizures occur because small numbers of neurons discharge abnormally. Anything that disrupts the normal homeostasis of the neuron and disturbs its stability may trigger abnormal

activity and seizures. A genetic predisposition to seizures has been suggested.

The causes of seizures in the elderly may be multifactorial and include cerebrovascular

disease (both ischemic and hemorrhagic stroke), neurodegenerative disorders, tumor, head trauma, metabolic disorders, and CNS infections. In some cases, if an etiology can be found and corrected, the patient will not require chronic AED treatment. The incidence of idiopathic epilepsy is higher in children. Many factors have been shown to precipitate seizures in susceptible individuals. A careful history should be obtained from patients presenting

with seizures because theophylline, alcohol, high dose phenothiazines, antidepressants (especially maprotiline or bupropion), and street drug use have been associated with provoking seizures. Children who are small for gestational age or with neonatal seizures are also at increased risk for developing epilepsy. The most clearly established risk factors for epilepsy in all age groups are head trauma (especially in patients in whom the dura mater has been breached and in whom there is evidence of loss of consciousness), CNS infections, and stroke. Immunizations have not been associated with an increased risk of epilepsy.

CLASSIFICATIONS:

I. Partial seizures (seizures begin locally)

A. Simple (without impairment of consciousness)

1. with motor symptoms
2. with special sensory or somatic sensory symptoms
3. with psychic symptoms

B. Complex (with impairment of consciousness)

1. Simple partial onset followed by impairment of consciousness—with or without automatisms
2. Impaired consciousness at onset—with or without automatisms

C. Secondarily generalized (partial onset evolving to generalized tonic-clonic seizures)

II. Generalized seizures (bilaterally symmetrical and without local onset)

- A. Absence
- B. Myoclonic
- C. Clonic
- D. Tonic
- E. Tonic-clonic
- F. Atonic
- G. Infantile spasms

III. Unclassified seizures

IV. Status epilepticus.

PATHOPHYSIOLOGY:

Seizures result from excessive excitation, or from disordered inhibition of a population of neurons. Initially, a small number of neurons fire abnormally. Then normal membrane conductances and inhibitory synaptic currents break down, excitability spreads locally (focal seizure) or more widely (generalized seizure).

Mechanisms that may contribute to synchronous hyper excitability include:

- Alterations of ion channels in neuronal membranes
- Biochemical modifications of receptors
- Modulation of second messaging systems and gene expression
- Changes in extracellular ion concentrations
- Alterations in neurotransmitter uptake and metabolism in glial cells
- Modification in the ratio and function of inhibitory circuits
- Local neurotransmitter imbalances (e.g., glutamate, γ -aminobutyric acid [GABA]),

acetylcholine, norepinephrine, and serotonin) Large numbers of generalized tonic-clonic (GTC) seizures (more than 100) and multiple episodes of status epilepticus may be associated with neuronal damage. In particular, continued exposure to glutamate may contribute to neuronal damage.

SCOPE OF DRUG UTILIZATION EVALUATION:

Studies on the process of drug utilization focus on factors related to prescribing, dispensing, administering and taking of medication, and its associated events, covering the medical and nonmedical determinants of drug utilization, the effects of drug utilization, as well as studies of how drug utilization relates to the effects of drug use, beneficial or adverse. Drug use evaluation (DUE) or DU studies is an ongoing, authorized and systematic quality improvement process, which is designed to:

- Review drug use and/or prescribing patterns.
- Provide feedback of results to clinicians.

- Develop criteria and standards which describe optimal drug use.
- Promote appropriate drug use through education and other interventions. They observe the patterns of drug use with current recommendations or guidelines for the treatment of a certain disease.
- They provide feedback of drug utilization data to prescribers.
- They relate the number of cases of adverse effects to the number of patients exposed.
- If it is possible to detect that the reaction is more common in a certain age group, in certain conditions or at a special dose level, then information on proper use of drug can be improved such as indications, contraindications, appropriate dose etc. so that withdrawal of drug may be avoided. They evaluate drug use at a population level, according to age, sex, social class etc.
- They include concept of appropriateness that must be assessed relative to the indication for the treatment, concomitant diseases (that might contraindicate or interfere with chosen drug therapy) and the use of other drugs (interactions). Thus they document the extent of inappropriate prescribing of drugs and also the associated adverse, clinical, ecological and economic consequences. Thus DUE plays a key role in helping the healthcare system to understand, interpret and improve the prescribing, administration and use of medications.
- The principal aim of DUE research is to facilitate rational use of drugs, which implies the prescription of a well-documented drug in an optimal dose on the right indication, with correct information and at an affordable price. It also provides insight into the efficacy of drug use i.e. whether a certain drug therapy provides value for money. DU

research can thus help to set priorities for the rational allocation of health care budgets.

- Epilepsy is a common, chronic neurological disorder characterized by recurrent[two or more] episodic paroxysmal involuntary clinical events associated with abnormal electrical activity from the neuron, which requires long term management and imposes a large burden on health care system. AEDs are also commonly used therapy for other conditions like prophylaxis for a manic depressive disorder, to relieve neurologic pain, and many more conditions apart from epilepsy. In epilepsy patients have to take medication for a long duration, sometimes lifelong. So the patient is at risk for numerous drug interactions. Drug utilization studies give us an insight to the drug usage among patients and help us to decide the rationality of such use. Irrational prescribing can lead to therapeutic failures, unwarranted adverse effects and rational economic burden on the patients.

MATERIALS AND METHODOLOGY:

STUDY SITE:

The study was conducted in paediatric department of Maharaja institute of medical sciences, Nellimarla, Vizianagaram.

STUDY PERIOD:

The study was conducted for a period of 6 months from December 2020 to May 2021.

STUDY DESIGN:

Prospective interventional analytical study.

SAMPLE SIZE:

A total of 100 cases will be included in the study.

STUDY CRITERIA:

INCLUSION CRITERIA:

- Patient of either sex attending paediatric department, receiving anti-epileptic drugs in any form.

- All the paediatric patients of age between 0-18 years and who were on antiepileptic drugs in paediatric inpatient and outpatient department of MIMS.

EXCLUSION CRITERIA:

- Patients above the age 18 years were excluded from the study.
- Patients whose parents are not willing to participate in the study were excluded.

STUDY PROCEDURE:

Initial sample size collected is 120

After elimination of all the missing data the final sample size 100 (The missing data is due to sudden discharge, or incomplete data)

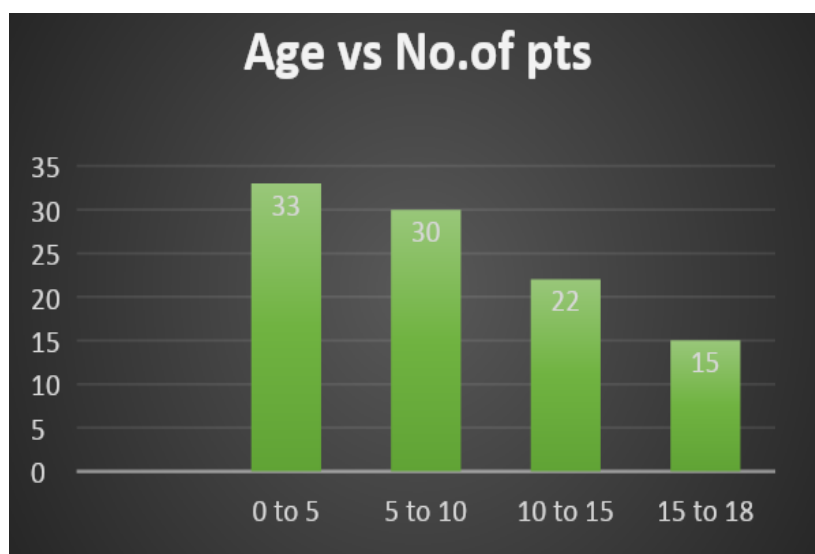
Preparation of standard questionnaire for

Filling the data through direct patient interaction

RESULTS:

Table 1: Age wise distribution of patients

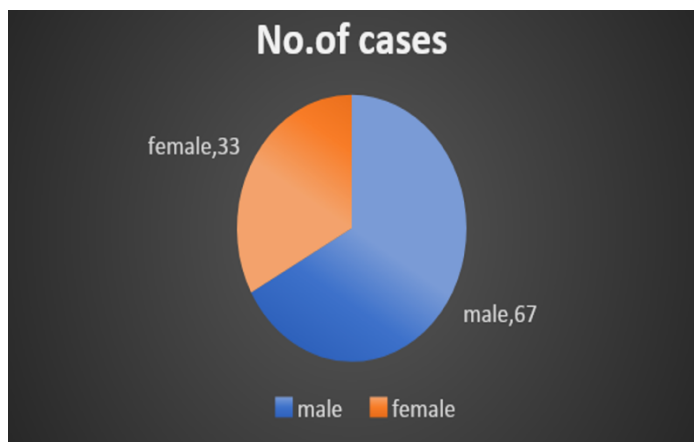
| Age | No. of patients |
|-------|-----------------|
| 0-5 | 33 |
| 5-10 | 30 |
| 10-15 | 22 |
| 15-18 | 15 |



Graph 1: Age wise distribution of patients

Table 2: Gender wise distribution

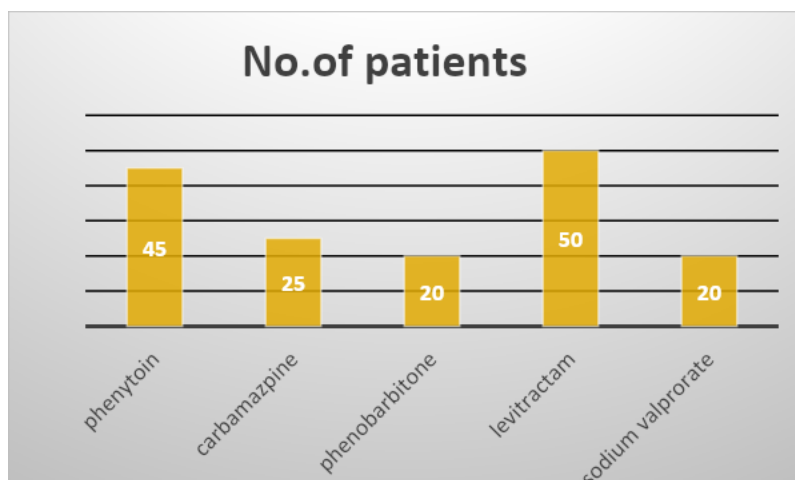
| Gender | No. of cases |
|--------|--------------|
| Male | 67 |
| Female | 33 |



Graph 2: Gender wise distribution

Table 3: Total no. of AEDS prescribed

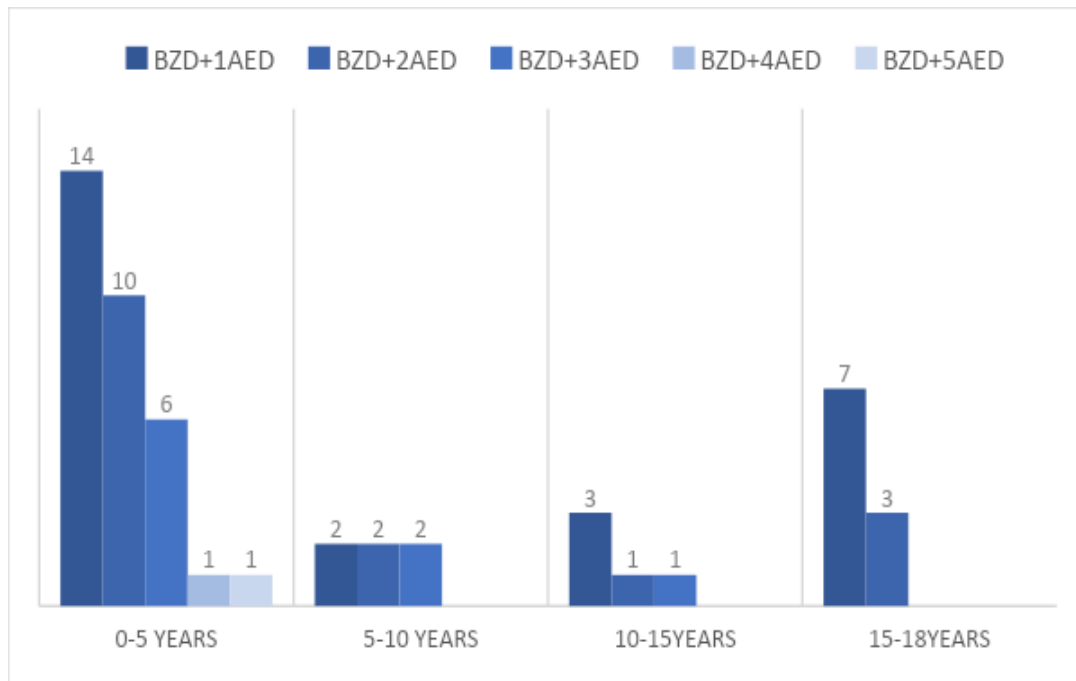
| AED'S | No. of patients |
|------------------|-----------------|
| Phenytoin | 45 |
| Carbamazepine | 25 |
| Phenobarbitone | 20 |
| Levetiracetam | 50 |
| Sodium valproate | 20 |



Graph 3: Total no. of AEDS prescribed

Table 4: Total no. of patients with combination therapy with AED'S

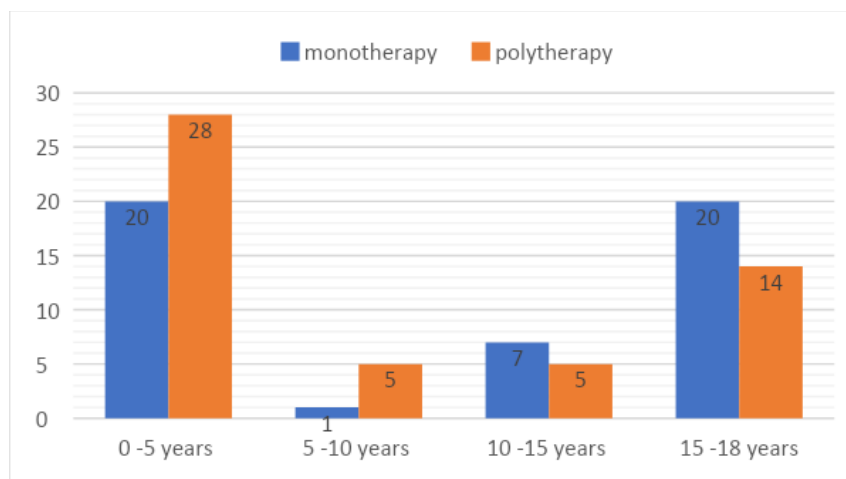
| Treatment given | 0-5 years | 5-10 years | 10-15 years | 15-18 years |
|-----------------|-----------|------------|-------------|-------------|
| BZD+1AED | 14 | 02 | 03 | 07 |
| BZD+2AED | 10 | 02 | 01 | 03 |
| BZD+3AED | 06 | 02 | 01 | 00 |
| BZD+4AED | 01 | 00 | 00 | 00 |
| BZD+5 AED | 01 | 00 | 00 | 01 |
| TOTAL | 32 | 06 | 05 | 11 |



Graph 4: Total no. of patients with combination therapy with AED'S

Table 5: Total no. of patients with types of AED therapy according to age

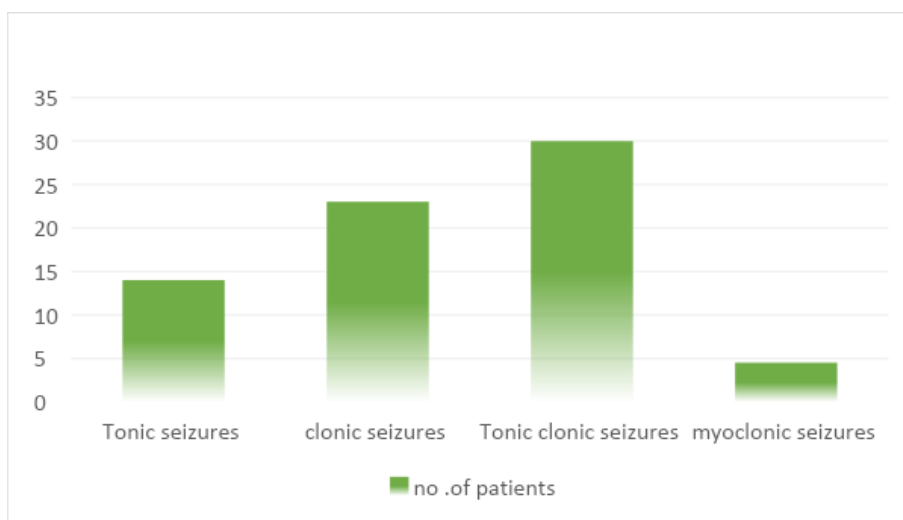
| Types of AED therapy | 0-5 years | 5-10 years | 10-15 years | 15-18 years |
|----------------------|-----------|------------|-------------|-------------|
| Monotherapy | 20 | 01 | 07 | 20 |
| Polytherapy | 28 | 05 | 05 | 14 |
| Total | 48 | 06 | 12 | 34 |



Graph 5: Total no. of patients with types of AED therapy according to age

Table 6: Total no. of patients with types of seizures

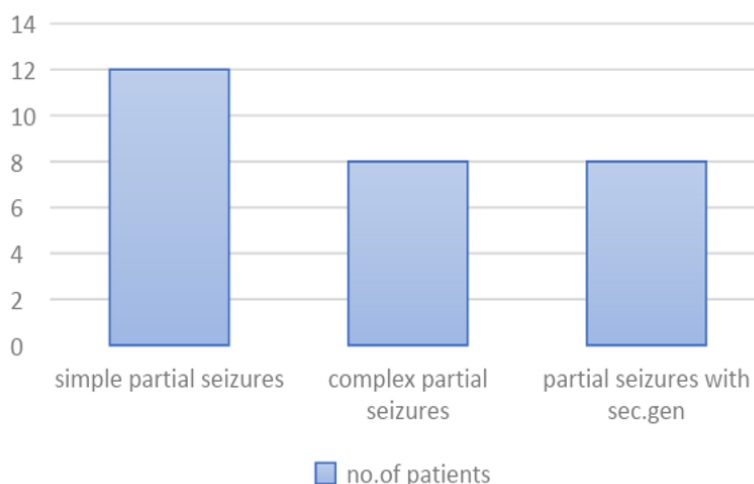
| Generalized seizures | No. of patients |
|-----------------------|-----------------|
| Tonic seizures | 14 |
| Clonic seizures | 23 |
| Tonic clonic seizures | 30 |
| Myoclonic seizures | 05 |
| Total | 72 |



Graph 6: Total no. of patients with types of seizures

Table 7:

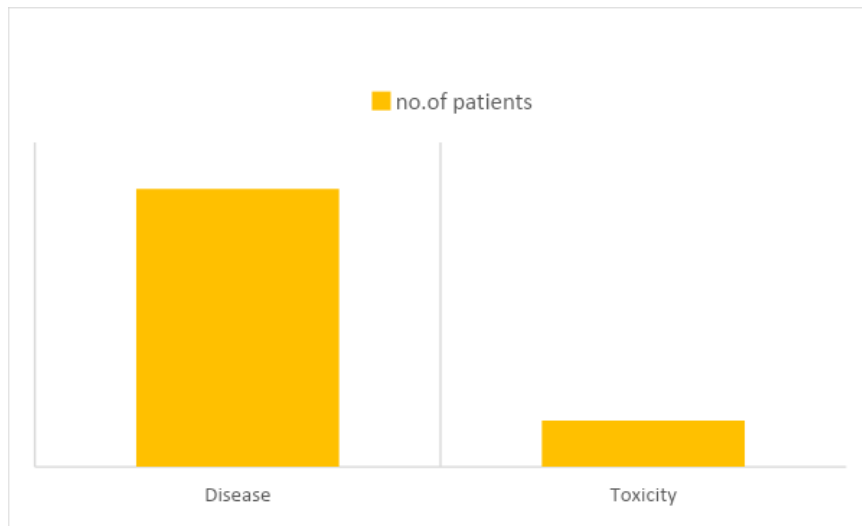
| Partial seizures | No .of patients |
|--|-----------------|
| Simple partial seizures | 12 |
| Complex partial seizures | 08 |
| Partial seizures with secondary generalization | 08 |
| Total | 28 |



Graph 7:

Table 8: No. of seizures patients with secondary causes

| Seizures due to secondary causes | No .of patients |
|----------------------------------|-----------------|
| Disease | 12 |
| Toxicity | 03 |



Graph 8: No .of seizures patients with secondary causes

Table 9: Total no. of patients with types of onset

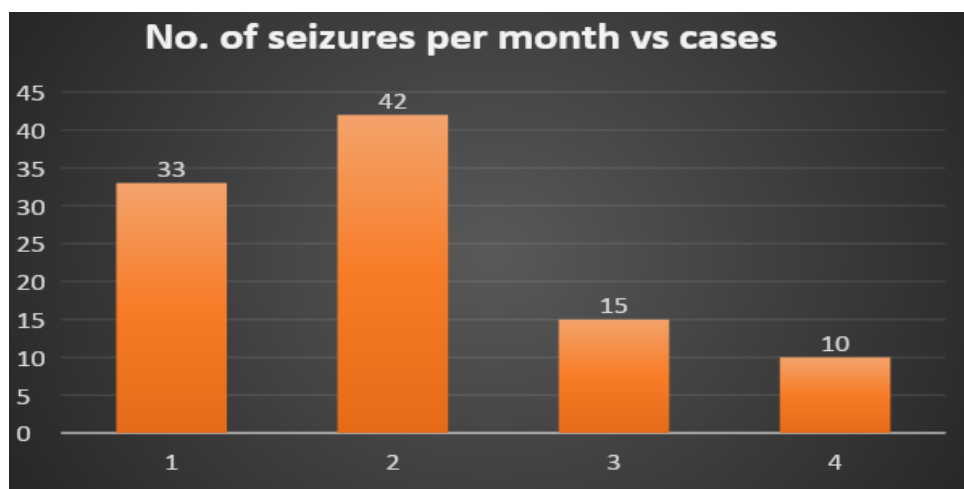
| Types of onset | No .of patients |
|----------------|-----------------|
| Established | 16 |
| Recurrent | 32 |
| New onset | 62 |

Table 10: Total no. of patients with different Etiology

| Etiology | No.of patients |
|------------------|----------------|
| Primary causes | 64 |
| Secondary causes | 36 |

Table 11: No. of seizures episodes per month before antiepileptic drug therapy

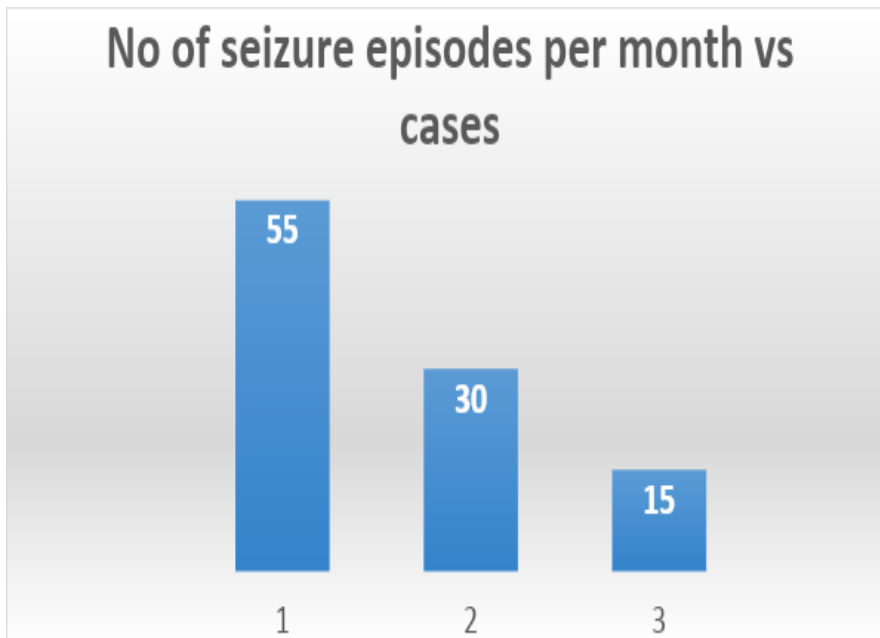
| No of seizure episodes per month | No of cases |
|------------------------------------|-------------|
| 1-2 episodes of seizures per month | 33 |
| 3-5 episodes per month | 42 |
| 6-8 episodes per month | 15 |
| >8 episodes per month | 10 |



Graph 9: No. of seizures episodes per month before antiepileptic drug therapy

Table 12: No. of seizure episodes per month after antiepileptic drug therapy

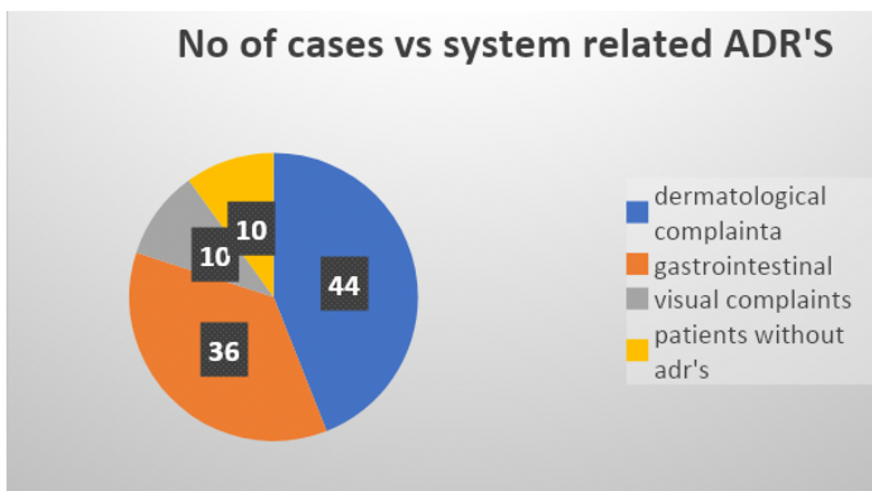
| No of seizure episodes per month | No of cases |
|------------------------------------|-------------|
| Seizure free patients | 55 |
| 1-2 episodes of seizures per month | 30 |
| 3-4 episodes of seizures per month | 15 |



Graph 10: No. of seizure episodes per month after antiepileptic drug therapy

Table 13: Other system related ADR'S to patients after antiepileptic drug therapy

| ADR'S | No. of cases |
|-----------------------------|--------------|
| Dermatological complaints | 44 |
| Gastrointestinal complaints | 36 |
| Visual complaints | 10 |
| Patients without ADR'S | 10 |



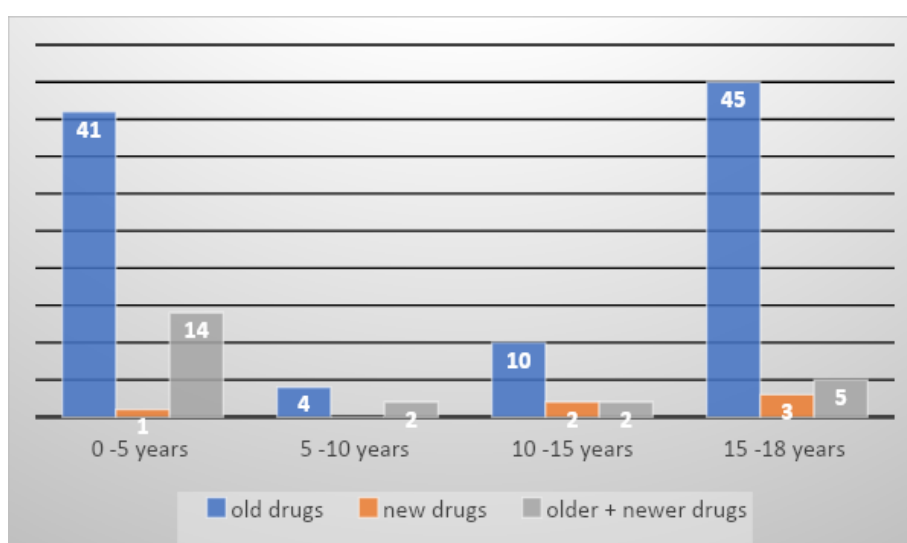
Graph 11: Other system related ADR'S to patients after antiepileptic drug therapy

Table 14: Total no. of patients with adverse effects

| S.no | Adverse effects | No of patients |
|------|------------------|----------------|
| 1. | Headache | 32 |
| 2. | Irritability | 09 |
| 3. | Hypersomnia | 04 |
| 4. | Confusion | 02 |
| 5. | Depressed mood | 02 |
| 6. | Weakness | 03 |
| 7. | Forgetfulness | 04 |
| 8. | Skin rash | 03 |
| 9. | Nightmare | 02 |
| 10. | Polyphagia | 01 |
| 11. | Vomit | 03 |
| 12. | Lack of appetite | 02 |
| | Total | 67 |

Table 15: Utilization pattern of AED as older, newer and older with newer AED

| AGE | Older drugs | Newer drugs | Older +newer drugs |
|------------|-------------|-------------|--------------------|
| 0-5 years | 41 | 01 | 14 |
| 5-10 years | 04 | 00 | 02 |
| 10-15years | 10 | 00 | 02 |
| 15-18years | 45 | 02 | 05 |
| Total | 100 | 03 | 23 |

**Graph 12: Utilization pattern of AED as older, newer and older with newer AED****DISCUSSION:****AGE DISTRIBUTION:**

In our study we frequently found the patients with age group 0-5 years (N=33) have frequent seizures compared with other group of patients i.e; 6 to 10 years and 10 to 15 years and 15 to 18 years, this is in contrast to the study conducted by Hirenkumar H.Dave who concluded that

patients of 6 to 10 years age suffered the most followed by 0-5 years .

GENDER DISTRIBUTION :

Among 100 patients studied we saw males (N=67) were predominant than females (N=33), in contrast with the study conducted by sharvani Hugara, showed females

were more frequently attacked with epilepsy compared with males.

DRUG UTILIZATION EVALUATION OF ANTIEPILEPTIC DRUGS:

There are above 20 antiepileptic drugs which are available in clinical use today in our hospital only 5 different antiepileptic drugs were used. The study highlighted that phenytoin was most commonly prescribed antiepileptic drug. Similar results obtained by Sobhana et al, mentioned that sodium valproate was most commonly prescribed followed by phenytoin and other drugs.

DUAL THERAPY DRUG DISTRIBUTION:

In our study, we discussed that patients with phenytoin with phenobarbitone/sodium valproate in combination therapy were most commonly observed, in contrast with the study conducted by Jincy George, mentioned that sodium valproate with levetiracetam/lorazepam combination therapy was most common.

MONOTHERAPY VS POLYTHERAPY:

In our study we found that between the age group of 0-5 years, 48 are with both monotherapy and polytherapy compared with age group of 15-18 years, 34 were with monotherapy and polytherapy. Out of these polytherapy was most common in all group of patients, in contrast with Jincy George, monotherapy was most common compared with polytherapy.

TYPES OF SEIZURES:

Among 100 patients, Generalized tonic clonic seizures (GTCs) were most common compared with other generalized seizures. In partial seizures, simple partial seizures were most common compared with other partial seizures. In contrast with Jincy George, generalized tonic seizures were most common compared to the generalized tonic clonic.

ETIOLOGY:

Among 100 patients of study, 64 patients are with primary causes of seizures and 36 patients are with secondary causes of seizures. In contrast with Julia Jose, 46 patients are with

primary cause of seizures and 46 patients are with secondary causes of seizures.

TYPE OF ONSET & SECONDARY CAUSE:

In our study population, new onset of patients (62) were more common compared with established and recurrent types of onsets. Primary causes are more in patients compared with secondary causes in contrast with Divya Ashok Kulkarni, secondary causes are more than primary causes.

EPISODES OF SEIZURES:

In our study of 100 patients, 3 to 5 episodes of seizures are more common before antiepileptic drug therapy and seizure free patients are more common after the antiepileptic drug therapy.

ADVERSE DRUG REACTIONS:

Among a total of 100 patients, 67 patients are with adverse reactions, out of 67 patients, 32 patients are with headache and other system related adverse drug reactions like dermatological complaints are more common in patients with antiepileptic therapy.

UTILIZATION PATTERN OF AED'S:

Among the age group of 0 to 18 years, 100 patients are with older drugs and 3 patients are with newer drugs and 23 patients are with both the newer and older drugs.

CONCLUSION:

Based on the result, we concluded that,

- Patients of age group 0-5 years suffered the most.
- Most males suffer with episodes of seizures.
- Phenytoin is the common drug given to patients.
- Among the age group of 0 to 5 yrs are with combination therapy with anti epileptic drugs.
- Polytherapy was more common in patients with anti epileptic drug therapy
- In seizures, generalized tonic clonic seizures are more common compared with partial seizures.

- Before antiepileptic drug treatment ,3-5 episodes of seizure per month are most common
- After antiepileptic drug treatment, seizure patients are most common
- Dermatological complaints and gastrointestinal complaints are most common in patients with antiepileptic drug treatment.

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