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## Pattern of Usage of Anti Epileptic Drugs In A Tertiary Neuro Care Unit In India

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### ABSTRACT

Epilepsy is a disorder that is best viewed as symptoms of disturbed electrical activity in the brain, which may be caused by a wide variety of etiologies. It is a collection of many different types of seizures that vary widely in severity appearance, cause, consequence an management. The present study was done to evaluate, which drug is more effective than the other AED, used in tertiary care hospital. We studied and analyzed the pattern usage of AED in tertiary care hospital. And evaluated the incidence of side effects of these drugs on the subjects in the study, studied the compliance to various recommendations/protocols for usage of AED in neurology intensive care unit, and also compared the commonest and least common anti epilepsy drugs in neurology care unit. Commonest drugs use in TBI, CVA, SAH, average age of patients having seizures. The required information was collected from the case sheets of individual patients in the designed data collection form. Patient details were collected through self designed, by patient interview, by prescriptions or by medication charts. The efficacy study conducted and was evaluated according to the declaration of "HELSIKI" (as embedded 1996) an by the incidence of adverse event reported by the patients.

**Keywords:** Epilepsy, AED, Efficacy, Adverse events, Seizures, Neuro care unit, Compliance, Incidence, Analyze, TBI, CVA, SAH.

### Abbreviations:

AED: Anti Epileptic Drugs, TBI: Traumatic Brain Injury, CVA: Cerebro Vascular Accident, SAH: Subarachnoid Haemorrhage, EEG: Electro Encephalo Gram

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## INTRODUCTION

Epilepsy is a disorder that is best viewed as a symptom of disturbed electrical activity in the brain, which may be caused by a wide variety of etiologies. It is a collection of many different types of seizures that vary widely in severity, appearance, cause, consequence, and management. It is also important to recognize that seizures can be just one (albeit the most obvious) symptom of an epileptic disorder. Patients with epilepsy also may display neurodevelopmental delay, memory problems, and/or cognitive impairment<sup>1</sup>. Each year, 120 per 100,000 people in the United States come to medical attention because of a newly recognized seizure. Epilepsy is a chronic disorder characterized by recurrent unprovoked seizures. The age-adjusted incidence of epilepsy is 44 per 100,000 person-years. Seizures occur because a group of cortical neurons discharge abnormally in synchrony. Anything that disrupts the normal homeostasis of neurons and their stability can trigger hyper excitability and seizures<sup>2</sup>. There are thousands of medical conditions that can cause epilepsy, from genetic mutations to traumatic brain injury. A genetic predisposition to seizures has been observed in many forms of primary generalized epilepsy. Patients with mental retardation, cerebral palsy, head injury, or strokes are at an increased risk for seizures and epilepsy<sup>3,4</sup>.

The more profound the degree of mental retardation as measured by the intelligence quotient (IQ), the greater is the incidence of epilepsy. In the elderly, seizures are primarily of partial onset associated with the focal neuronal injury induced by strokes, neuro-degenerative disorders (e.g., Alzheimer disease), and other conditions. Idiopathic etiology is the term used for suspected primary generalized seizures, whereas cryptogenic etiology is used if no obvious cause is found for partial-onset seizures. The incidence of idiopathic epilepsy is higher in children<sup>5</sup>. Hyperventilation can precipitate absence seizures. Sleep, sleep deprivation, sensory stimuli, and emotional stress increase the frequency of seizures. Perinatal injuries and small gestational weight at birth are also risk factors for the development of partial-onset seizures<sup>6,7</sup>.

### **Pathophysiology:**

Seizures result from excessive excitation or in the case of absence seizures from disordered inhibition of a large population of cortical neurons. The clinical manifestations depend on the site of the focus, the degree of irritability of the surrounding area of the brain, and the intensity of the impulse. There are multiple mechanisms that might contribute to synchronous hyper excitability including:

- (1) Alterations in the distribution, number, type and biophysical properties of ion channels in the neuronal membranes;
- (2) Biochemical modifications of receptors;
- (3) Modulation of second messaging systems and gene expression;
- (4) Changes in extracellular ion concentrations;
- (5) Alterations in neurotransmitter uptake and metabolism in glial cells; and
- (6) Modifications in the ratio and function of inhibitory circuits<sup>8,9</sup>.

However, transitory imbalances between the main neurotransmitters, glutamate (excitatory) and  $\gamma$ -aminobutyric-acid (GABA) (inhibitory), and neuromodulators (e.g., acetylcholine, norepinephrine, and serotonin) might play a role in precipitating seizures in susceptible patients<sup>10</sup>.

### **Clinical Presentation:**

The International Classification of Epileptic Seizures combines the clinical description with certain electrophysiologic findings to classify epileptic seizures. Seizures are divided into two main pathophysiologic groups—partial seizures and generalized seizures by EEG recordings and clinical symptomatology. Partial (focal) seizures begin in one hemisphere of the brain and—unless they become secondarily generalized result in an asymmetric motor manifestation<sup>11</sup>. Partial seizures manifest as alterations in motor functions, sensory or somatosensory symptoms, or automatisms. Partial seizures with no loss of consciousness are classified as simple partial (SP). Partial seizures with an alteration of consciousness are described as complex partial (CP). With CP seizures, the patient can have automatisms, periods of memory loss, or aberrations of behaviour. Some patients with CP epilepsy have been mistakenly diagnosed as having psychotic episodes. Generalized seizures have clinical manifestations that indicate involvement of both hemispheres. Generalized absence seizures are manifested by a sudden onset, interruption of ongoing activities, a blank stare, and possibly a brief upward rotation of the eyes. They generally occur in young children through adolescence. It is important to differentiate absence seizures from complex partial seizures<sup>12</sup>.

### **General**

In most cases, the healthcare provider will not be in a position to witness a seizure. Many patients (particularly those with CP or GTC seizures) are amnesic to the actual seizure event. Obtaining an adequate history and description of the ictal event (including time course) from a third party (e.g., significant other, family member, or witness) is critically important. With treatment the typical clinical presentation of the seizure may change<sup>13,14</sup>.

### **Symptoms**

Symptoms of a specific seizure will depend on seizure type. Although seizures can vary between patients, they tend to be stereotyped within an individual.

- CP seizures can include somatosensory or focal motor features.
- CP seizures are associated with altered consciousness.
- Absence seizures can be almost nondetectable with only very brief (seconds) periods of altered consciousness.
- GTC seizures are major convulsive episodes and are always associated with a loss of consciousness<sup>15</sup>.

### Signs

Interictally (between seizure episodes), there are typically no objective or pathognomonic signs<sup>16</sup>.

Anti convulsants are also known as anti epileptic drugs or anti seizure drugs are a group of pharmacological agents used in treatment of epileptic seizures. Anti convulsants are also increasingly used in the treatment of bipolar disorder and borderline personality disorder. Since many seen to act as mood stabilizers and for treatment of neuropathic pain. Anti convulsants are accurately called as Anti-epileptic drugs and are often referred to as anti seizures drugs because they provide symptomatic treatment only and have not been demonstrated to alter the course of epilepsy. The etiology of seizure is multi factorial in any given individual. There are factors such as head injury and infection for which a clear and substantial risk for epilepsy has been established and a direct casual relationship could be assessed. It is estimated that the overall “incidence” of epilepsy (number of new cases observed over a fixed period of time) lies between 20 - 50 cases per year per 100,000 persons in a general population. The usual “prevalence” rate (number of persons with epilepsy during a specified time) is 500-1000 cases per 100,000 persons in the population. Going by these statistics, there will be about 200,000 to 500,000 new cases in the whole of India (estimated population about 100 crores)<sup>17,18</sup>.

The following practical points need to be remembered:

- One in 20 people will have an epileptic seizure at some point in their lives.
- One in 100-200 people in a general population has epilepsy at any given time.
- About 50–70% patients will develop epilepsy (have their first seizure) before the age of 18 years.

Use of anti epileptic drugs is increasing day by day in the conditions other than epilepsy. As the Anti epileptic drugs are used mainly for the treatment of epilepsy. Most of the anti epileptic drugs are used for treatment other than epilepsy based on their mechanism of action and the efficacy of

the drugs. This study was done mainly to list the anti epileptic drugs which are used in epilepsy and the epileptic drugs which are used for other than epilepsy conditions. Different anti epileptic drugs are used in different conditions as their main mechanism of action is the potentiation of gamma-aminobutyric acid mediated inhibition, inactivation of sodium or calcium channels, and blockade of N-methyl-D-aspartate receptors. Inactivation of sodium channels by antiepileptic drugs may reduce ectopic discharge from injured nerve endings and neurons of dorsal root ganglia. This leads to decrease in the abnormal neuronal discharge in the central nervous system<sup>19</sup>.

AED's are the main stay for the therapeutic management and prophylaxis of seizures. A myriad of drugs have come into use with better therapeutic profile as compared to the previous ones which had numerous side effects. In this study we instead to look into the various AED's commonly used in a tertiary acute neuro care unit<sup>20</sup>.

Our present study is to evaluate which drug is more effective than the other antiepileptic drugs used in tertiary hospitals.

**Primary objective:**

- To study and analyze the pattern and usage of AED in a tertiary care hospital.
- To study the incidence of side effects of these drugs on subjects in the study.
- To study the compliance to various recommendations / protocols for usage of AED in neuro intensive care unit.

**Secondary objectives:**

- To find the commonest and least common anti-seizure drug in neuro care unit.
- Commonest drug used in TBI, CVA, SAH.
- Second commonest drug used in the incidence of seizures.
- Average age of patients having seizures.

## MATERIALS AND METHOD

**Patient selection:**

**Inclusion criteria-**

- All patients admitted to the acute neuro care unit irrespective of age, sex, pre surgery, post surgery and other conditions.
- Diseases of central nervous system have been included in the study.

**Exclusion criteria**

- All patients admitted with diseases of peripheral nervous system are excluded in the study.
- ANCU admissions of diseases not pertaining to CNS.

**Designing a data collection form:**

A data collection form was designed to collect the patient's data including patient's personal details (name, age, sex, height, weight, address, marital status and occupation) family history, past medical history, complications and lifestyle modifications.

**Source of data:**

Patient's data relevant to study was obtained from the following resources

- Data collection form.
- Treatment chart
- Direct patient interview

**Collection of data:**

The required information was collected from the case sheets of individual patients in designed data collection form. Patient details were collected through self-designed data collection form, by patient interview, by prescriptions or medication chart, patient data collection include

- Patient's demographics details.
- Co-morbid conditions.
- Post medical and medication history.
- Present medication.
- Patient compliance.

**Efficacy and safety evaluation:**

- The study was conducted according to the declaration of Helsinki (as amended in 1996) and Good Clinical Practice Guideline.
- Ethical committee approval has been obtained from independent ethical the institution where the study is being performed.
- Written informed consent was obtained from all the patients before enrollment into the study.
- Safety and efficacy were evaluated by incidence of adverse event reported by the patients.

**Sample size:**

As the antiepileptic drugs are used in patients a limited sample of 60 patients admitted to Yashoda hospital were taken into consideration. There were 60 patients available from our study center.

**Statistical analysis:**

The descriptive analysis was done by using all the demographic data collected in the sample. The data was collected for 60 days in the hospital in all the patients who are receiving the anti epileptic drugs with or without seizures.

## RESULTS AND DISCUSSION

A total of 60 patients were included in our study at Yashoda hospital, Secunderabad. All the patients who are being treated with the anti epileptic drugs are included in the study. All patients admitted to the acute neuro care unit irrespective of age, sex, pre surgery, post surgery and other conditions were included and the patients with the diseases of central nervous system are also included in the study. All the demographic data was collected and is converted into bar diagrams and pie charts. The Table-1 represents the frequency of the anti epileptic drugs used in the total study.

**Table 1: Frequency of the anti epileptic drugs used in the total study**

N= Patients included	Seizures	Gender	Age	Day	Dru g-1	Dru g-2	Dru g-3	Dru g-4	Dru g-5	Dru g-6	Dru g-7	Dru g-8
Valid	182	182	182	182	132	56	7	1	15	6	6	27
Missing	0	0	0	0	50	126	175	181	167	176	176	155

In the **Table 1** where,

Drug-1: Levipil,

Drug-2: Phenytoin,

Drug-3: Lacosamide,

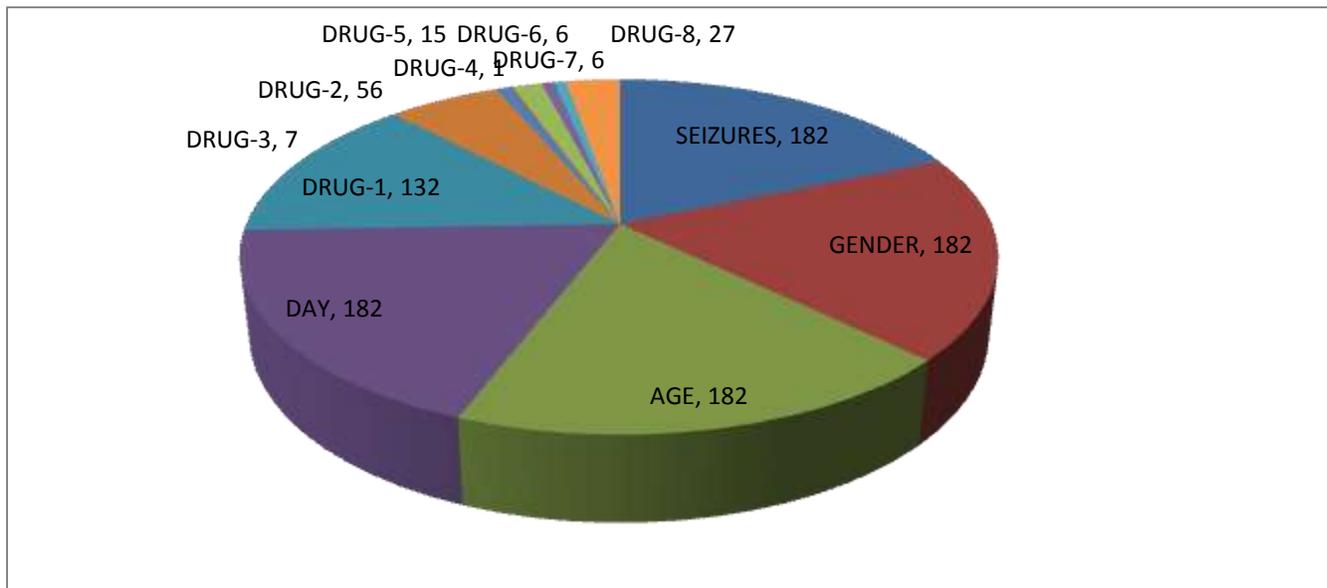
Drug-4: Phenobarbitol,

Drug-5: Lorazepam,

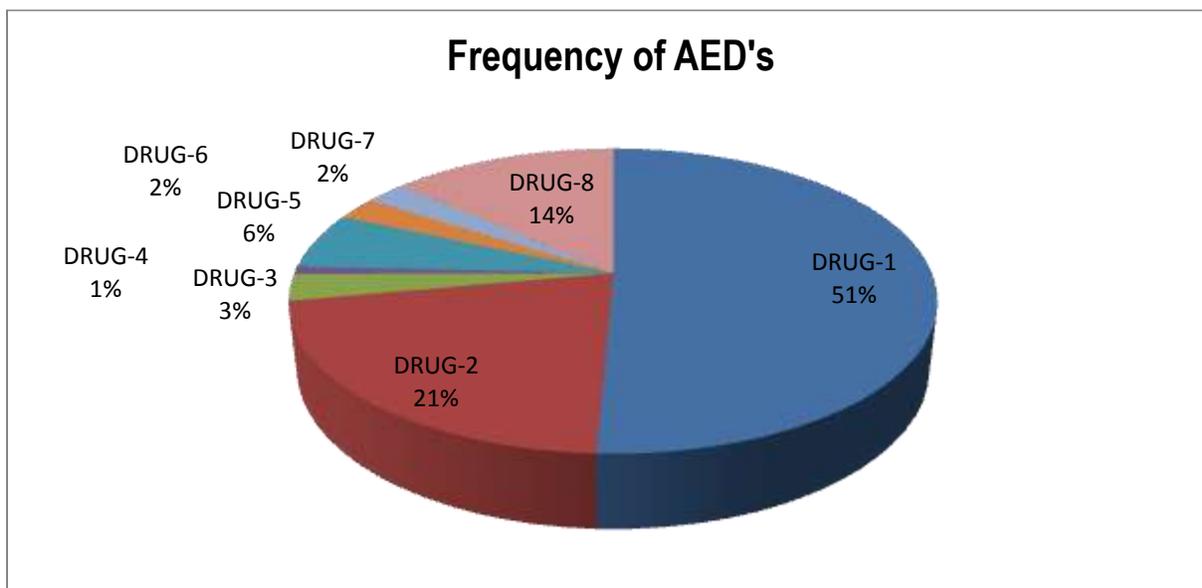
Drug-6: Carbamazepam,

Drug-7: Clonazepam,

Drug-8: Gabapentin.



**Figure 1: The pattern of AEDs frequencies**



**Figure 2: The percentage of drugs frequencies**

In the **Figures** where,

Drug-1: Levipil,

Drug-2: Phenytoin,

Drug-3: Lacosamide,

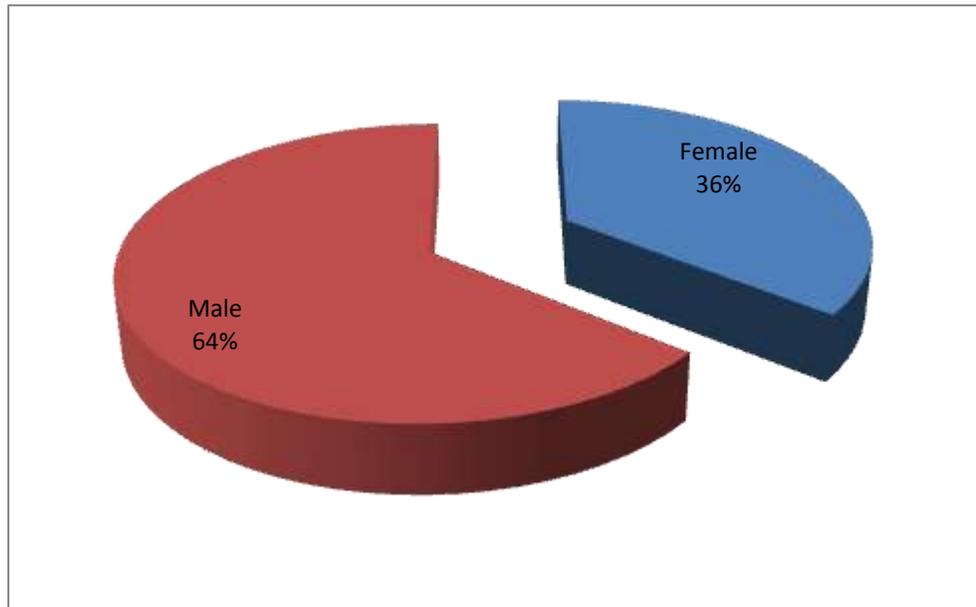
Drug-4: Phenobarbitol,

Drug-5: Lorazepam,

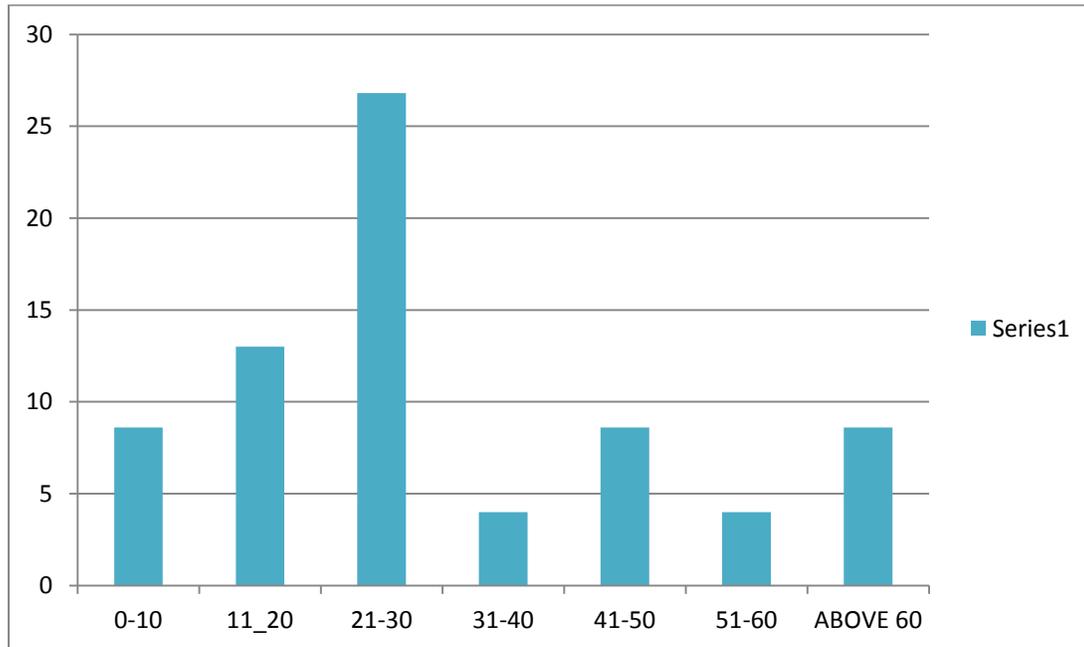
Drug-6: Carbamazepam,

Drug-7: Clonazepam,

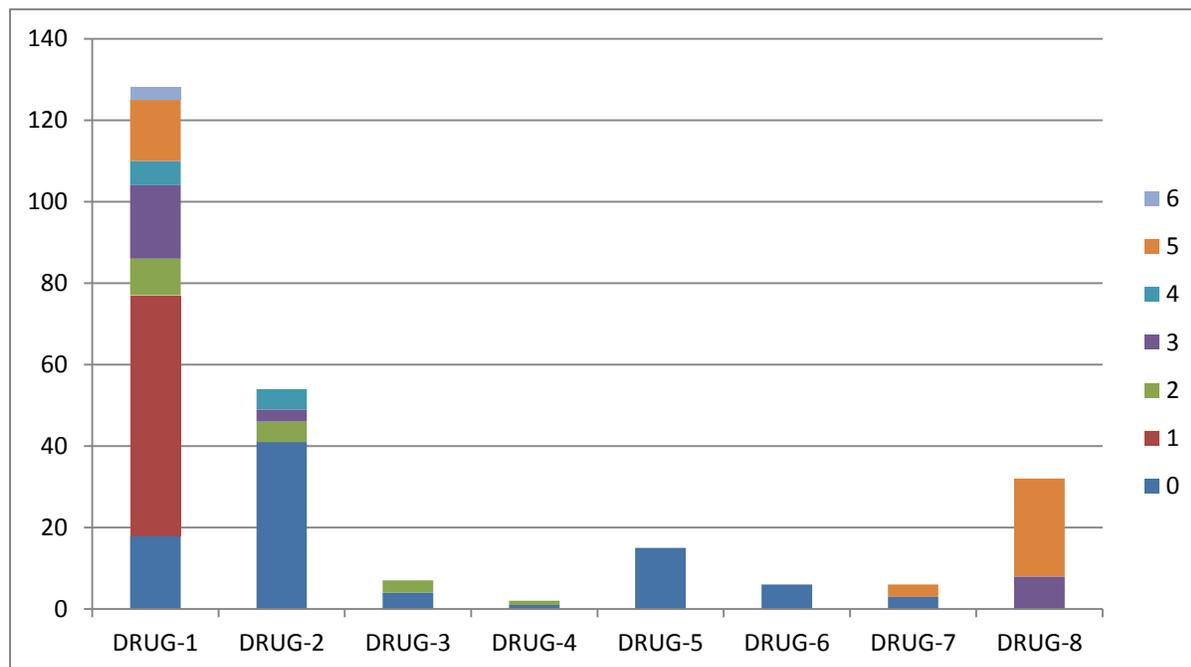
Drug-8: Gabapentin.



**Figure-3: The percentage of total male and female patients included in the study**



**Figure-4: The average age of the patients having seizures and average age where the seizures are most likely to occur**



**Figure-5: The commonest and the least common drug used in all conditions and the second commonest drug used**

In the **Figure-5** where,

0-No seizures,

1-Seizures,

2-Traumatic brain injury,

3-Cerebrovascular accident,

4-Subarachnoid hemorrhage,

5-Others,

6-Status epilepticus.

## CONCLUSION

In all the anti-epileptic drugs used drug-1 (Levetiracetam-51%) is the most commonly used and the drug-4 (Phenobarbital-1%) is the least commonly used drug. In all the epileptic drugs Drug-2 (Phenytoin-21%) is the second commonly used drug. The average age of patients having seizures was found to be 21-30. Drug-1 (Levetiracetam) and Drug-2 (Phenytoin) are commonly used drug in the condition-2 (TBI), condition-3 (Cerebrovascular accident) and in condition-4 (Subarachnoid haemorrhage). The average use of anti epileptic drugs with less reoccurrence and side effects are to be monitored in tertiary care unit hospitals for increased mortality rate.

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