ORIGINAL ARTICLE

INTERNATIONAL JOURNAL OF CLINICAL PHARMACOKINETICS AND MEDICAL SCIENCES
Published by Pharma Springs Publication Journal Home Page: https://pharmasprings.com/ijcpms/

Prescribing Patterns of Anticonvulsant Drugs in Epilepsy in a Tertiary care Hospital: An Observational Prospective Study

Dinesh Kumar Kukunuri*[1], Richard Noah[1], Sugreev Dwivedi Anuj[2], Sasi Karnati[3]

[1]H.K.E.S.S Mathosree Taradevi Rampure Institute of Pharmaceutical Sciences, Gulbarga-585105, Karnataka, India
[2]Parul Institute of Pharmacy and Research, Vadodara-391760, Gujarat, India
[3]Anesthesiology Department, Medicover Hospitals, Nellore-524003, Andhra Pradesh, India

Article History:

Received on: 02 Jun 2021
Revised on: 12 Jun 2021
Accepted on: 14 Jun 2021

Keywords:

Antiepileptic Drug, Prescribing Pattern, Polytherapy, Medication Adherence

ABSTRACT

There is a testimonial of various patterns of drug prescription of anticonvulsant drugs in India. The latest upcoming drugs are extensively available at present and the way of these newer drugs are prescribed is quite interesting to see. Complications in antiepileptic therapy such as the use of poly-therapy, adverse drug reactions, drug interactions, lack of medication adherence and so on, can be point out and cleared up by clinical pharmacist. On considering all these points, this study was commenced with the title: A study on prescribing patterns of anticonvulsant drugs in epilepsy in a tertiary care hospital. Prospective observational study of 6 months duration was carried out. Patients prescribed with anti-epileptic drugs in General Medicine and Neurology out-clinic department were selected according to inclusion criteria. Data were collected in the pre-prepared data collection form after obtaining the patient consent and verified the patient case sheets/ prescriptions. Morisky Medication Adherence Scale-8 (MMAS-8) was utilized to assess the medication adherence at baseline. Microsoft excel was used to summarize the analysis of data. Data were measured in percentage and frequency using descriptive statistics. For testing significant associations, Chi-square test was performed, where $P<0.05$ was considered as statistically significant. Usage of newer antiepileptic drugs was very less, with high evidence of polytherapy in the prescriptions for treating epilepsy. Clobazam was the most commonly prescribed drug. Medication adherence among these patients was less.

*Corresponding Author

Name: Dinesh Kumar Kukunuri
Phone: 9100554988
Email: dineshalliswell1998@gmail.com

eISSN: 2583-0953

DOI: https://doi.org/10.26452/ijcpms.v1i2.198

Production and Hosted by

Pharmasprings.com

© 2021 | All rights reserved.

INTRODUCTION

Seizure is a clinical incident occurs because of the abnormal electrical discharge in the brain. While, epilepsy is the proneness to have recurrent seizures [1]. Epilepsy is a clinical manifestation of a brain disorder rather than a disease itself [1]. An epileptic seizure is a short-term paroxysm of unrestrained discharge of neurons that bring about an event that is not noticeable by the person who having the seizure but can be detected by an observer. The inclination to have recurrent attacks is known as epilepsy [2].

Epileptic seizures or attacks are the symptoms of many other diseases. There are many causes for seizures or epilepsy. Further epilepsy is classified into many categories. Recurrence is common with seizures. The recurrence rate after first seizure approaches 70% during first year, most of the recur-

rent attacks occur within a month or two following the first attack. The recurrent attacks can be avoided if triggering factor is identified. The seizures that are prolonged or repetitive are associated with considerable morbidity and mortality. Patients with epilepsy experience other co-morbidities including depression, anxiety, neuro-endocrine disturbance, also may display neuro-developmental delay, memory issues and cognitive impairment [3].

Incidence and prevalence

Epilepsy is a common disorder. The incidence has been in the range of 20 - 70 cases per 100000 persons approximately, and the cumulative incidence at 2 -5%. The second raise is majorly due to cerebrovascular diseases. Most of the studies show that prevalence of active epilepsy between 4 -8 per thousand1000 [2]. The prevalence of epilepsy in European countries is about 0.5%. Prevalence is almost 5 times higher in the developing countries than in developed countries [1].

Classification

There are two types of seizures

Generalized onset seizures

These seizures influence the dual sides of the brain or groups of cells on dual sides of the brain at the exact timing. This term comprises seizures types like tonic-clonic, absence, or atonic and others [4].

Tonic-Clonic

Usually called grand mal attacks, these are the most common one of all epileptic seizures, without warns the patient and then suddenly goes stiff, falls and convulses along with salivation, cyanosis incontinence and tongue biting [1].

Absence

Usually called petit-mal, these are the rare one among generalized seizure, they occurs extensively in childhood and early adolescence, the child goes blank and stares, and flopping of the head occurs. This attack lasts only for a few seconds and then gone unnoticeable [5].

Myoclonic

These are abrupt, involuntary shock like jerks, which may involve the whole body or the arms or the head. They usually occur in the morning, shortly after waking. It is vital to know that there are other non-epileptic myoclonic jerks that occur in other diseases [6].

Atonic

These seizures are connected with the sudden loss of muscle tone, and then the person would collapse to the earth. They are rare, accounting for less than 1% of the epileptic seizures [1].

Focal onset seizures

The idiom focal is used preferably of incomplete to be more precise when speaking about where seizures can start. Focal seizures can begin in one place or group of cells in one side of the brain [7].

1. Focal Onset Aware Seizures
2. Focal Onset Impaired Awareness

Unknown onset seizures

When the origination of a seizure is not well-known, it's referred as an unknown onset seizure. A seizure could also be known an unknown onset if it's not observed or seen by anyone, for instance when seizures occurs at night or in a person who lives alone. When more information is collected, later an unknown onset seizure may be diagnosed as a focal or generalized seizure [7].

Etiology

The seizures are occurred due to the abnormal discharge of neurons that may be because of any pathological process which affects the brain. The idiopathic epilepsies are those in which there is a clear genetic component, and they probably account for a thread of all new cases of epilepsy. The term symptomatic epilepsy indicates that a probable cause has been identified [4].

The etiology of epilepsy based upon the age of the patient and the type of seizures. The most common causes in young infants are low o_2 levels or birth asphyxia, intracranial trauma during birth, metabolic disturbance and congenital malformation of brain or infection [4].

In young children and adolescents, idiopathic seizures accounts for the majority of the epilepsies, although trauma and infection also play an important role [4]. In children aged between6 months and 5 years, seizures may occur along with febrile illness [4].

Path-physiology

Normally brain electrical pursuit is non-synchronous [8] its activity is controlled by various factors both within the neuron and the cellular environment. Factors within the neuron comprises the type, number and distribution of ion channels, changes to receptors and changes of gene expression [9]. Factors around the neuron comprise ion concentrations, synaptic plasticity and synchronize of transmitter breakdown by glial

cells [9, 10]. Chronic inflammation also seems to play a role [11]. The exact procedure of epilepsy is unknown [12] and only little is known about its cellular and network mechanisms. However, it is unknown under which circumstances the brain transfers into the activity of a seizure with its excessive regulation [13, 14]. In epilepsy, the objection of excitatory neurons to fire during this period is reduced [8]. This evolve in a specific area from which seizures may develop is known as a "seizure focus" [8]. Another mechanism of epilepsy may be the up-regulation of excitatory circuits or down-regulation of inhibitory circuits following an injury to the brain [8, 15]. These secondary epilepsies occur through processes known as epileptogenesis [16, 17] . Failure of the blood–brain barrier may also be a causal procedure as it would permit substances in the blood to enter the brain [18].

Seizures

There is corroboration that epileptic seizures are often not an unplanned event. Seizures are usually brought on by factors like stress, alcohol abuse, flickering light, or a lack of sleep, among others. The idiom seizure threshold is generally employed to indicate the amount of stimulus needed to bring about a seizure. Seizure threshold is reduced in epilepsy [13].

In epileptic seizures a group of neurons start firing in an abnormal, excessive, and synchronized manner [8]. This result in a wave of depolarization called as a paroxysmal depolarizing shift [19]. Commonly, after an excitatory neuron fires it becomes more resistant to firing for a period of time. This is because of in part to the effect of inhibitory neurons, electrical changes within the excitatory neuron, and the negative effects of adenosine [8].

Focal seizures start in one hemisphere of the brain while generalized seizures begin in dual hemispheres [17]. Some types of seizures may alter the brain structure, while others seem to have a little effect [20]. Gliosis, neuronal loss, and atrophy of specific areas of the brain are connected to epilepsy but it is not clear if epilepsy results these alterations or if these changes will occurs in epilepsy [20].

Signs and symptoms

Several various symptoms can be seen during a seizure. These new classifications distinguish them simply into groups that imply the movement.

For generalized onset seizures

Motor symptoms may comprises sustained rhythmical jerking movements (clonic), muscles becoming weak or limp (atonic), muscles becoming tense or rigid (tonic), brief muscle twitching (myoclonus), or epileptic spasms (body flexes and extends repeatedly) [7].

Non-motor symptoms are often called absence seizures. These can be typical or atypical absence seizures (staring spells).

For focal onset seizures

Motor symptoms may also include jerking (clonic), muscles becoming limp or weak (atonic), tense or rigid muscles (tonic), brief muscle twitching (myoclonus), or epileptic spasms. There may be repeated automatic movements, like clapping or rubbing of hands, lip smacking or chewing, or running [7].

Non-motor symptoms include Examples of symptoms that don't affect movement could be seen such as changes in sensation, emotions, thinking or cognition, autonomic functions (such as gastrointestinal sensations, waves of heat or cold, goose bumps, heart racing, etc.), or lack of movement (called behavior arrest) [7].

For unknown onset seizures

Motor seizures are described as either tonic-clonic or epileptic spasms.

Non-motor seizures often comprises of a behavior arrest. This means that movement stops – the person may just stare and not make any other movements [7].

Diagnosis

Determining a right and precise diagnosis is needed prior to any confirmation of pharmacotherapy. When a patient complains of paroxysmal stereotypical spells that may be seizures, it must be obstinate if the spells are really seizures [21].

A proper diagnostic plan of a patient having with seizures should include:

1. Thorough neurologic examination
2. Electroencephalogram
3. Laboratory tests (CBC, LFT, Serum chemistry)
4. Neuro-imaging (preferably magnetic resonance imaging)

Patients with epilepsy may have totally normal results in their assessment. Many of tests are done to find the other causes of seizures. (eg: infection or electrolyte imbalance) [21].

Usually the EEG appears normal between seizures several manipulation can be done in a try to express seizure or seizure like activity on the EEG [21].

Table 1: Age wise distribution of the study participants

S. No	Age	Gender		Total	*P* value
		Male	Female		
1	15-19	17 (54.8%)	14 (45.2%)	31 (100%)	
2	20-29	19 (61.3%)	12 (38.7%)	31 (100%)	
3	30-39	7 (38.9%)	11 (61.1%)	18 (100%)	
4	40-49	6 (42.9)	8 (57.1%)	14 (100%)	0.0318*
5	50-59	1 (20%)	4 (80%)	5 (100%)	
6	60-69	1 (100%)	0 (0%)	1 (100%)	
Total		51 (51%)	49 (49%)	100 (100%)	

(*p<0.05 is statistically significant)

Table 2: Types of prescribed therapy among the study participants

Type of Therapy	No. of Subjects	Percentage
Single Therapy	44	44
Double Therapy	35	35
Triple Therapy	17	17
Quadruple Therapy	3	3
Quintuple Therapy	1	1

Table 3: Single drug therapy pattern of AED's prescription

S. No	Drug Prescribed	No. Sub (N=44)	%
1	Clobazam	0	0
2	Phenobarbitone	1	2.3
3	Carbamazepine	11	25.0
4	Divalproex Sodium	12	27.3
5	Phenytoin	7	15.9
6	Oxcarbazepine	4	9.1
7	Leviteracetam	9	20.4
8	Topiramate	0	0
9	Clonazepam	0	0
	Total	44	100

This comprises sleep deprivation, photic stimulations, prolonged (more than 20 mins) EEG recording and 24 hours EEG monitoring with video correlation.

Key points on diagnosis

1. Diagnosis to be made immediately by a specialist with an interest in epilepsy. EEG to be used to support diagnosis [2]; 2. MRI to be used in people to evolve epilepsy as adults, in whom focal onset is doubtful, or whom seizure persist [2].

Management

Pharmacological management

Barbiturates: Phenobarbital; Hydantoins: Phenytoin, Fosphenytoin; Iminostilbenes: Carbamazepine, Oxcarbazepine; Succinimides: Ethosuximide; Aliphatic Carboxylic Acids: Valproic Acid, Divalproex; Benzodiazepines: Clonazepam, Lorazepam, Diazepam, Clobazepam; Phenyltriazene: Lamotrigine; Cyclic GABA Analogue: Gabapentin, Pregabalin;

Newer Drugs: Vigabatrin, Topiramate, Leviteracetam, Tiagabin, Zonisamide

Non - Pharmacological management

Ketogenic diet and modified Atkins diet

Vagal nerve stimulation

Implantable neurostimulator

Aim of the Study

To Study the Prescribing Patterns of Anti - Convulsants in Epilepsy

Objectives

1. To study the trends in prescribing patterns of Anti - Convulsants in epilepsy.
2. To study the medication adherence.
3. To study the clinical profile.

Need of the Study

1. Epilepsy is the most common disease worldwide.
2. In U.S. 3.4 million number of patients and in India more than 12 million people are suffering from epilepsy.
3. AEDs are the Prescribing agents used in epilepsy
4. Now a days, a wide variety of AEDs are available in the market. So we are conducted a study on the current trends of prescribing patterns of AEDs.

METHODOLOGY

Study design: A prospective observational study; Study site: Department of Neurology/ Medicine of Medicover hospital, Nellore; Study duration: 6 months; Study size: 100 Epilepsy Patients

Inclusion Criteria

1. Patients above age group of 15 years.
2. All the patients of both genders with confirmed diagnosis of Epilepsy.
3. Patient who willing to participate in the study.

Exclusion Criteria

1. Patients above age group of 15 years.
2. All the patients of both genders with confirmed diagnosis of Epilepsy.
3. Patient who willing to participate in the study.

Study Materials

1. Patient data collection proforma
2. Patient informed consent form

Method of the Study

On daily basis patients who were came to Neurology department with the epilepsy complaints were screened as per the study eligibility criteria and eligible patients were recruited after getting the consent through written, signed ICF from the subjects/care takers. After identifying the subjects the eligible subjects, their complaints and severity and study the prescriptions based type of epilepsy and severity, prescribing various therapies, Such as Double drug therapy, triple drug therapy quadrant drug therapy and penta drug therapy. Patients were monitored for the prognosis through interview, monitoring vitals and to assess the adherence of patients. Patients' details along with outcomes of the treatment were observed and noted in a standard self designed data collection form. All the patients and their care takers were educated/ regarding lifestyle modifications to be followed.

Statistical Analysis

Data was analyzed by using Graph Pad Prism software to find out. P-value with 95% CI. Percentage, Average and SD was assessed by using Microsoft 2007 Excel data sheet.

RESULTS

Gender

In this study, out of 100 patients, gender distribution almost equal, where females were 51 and the remaining 49 were males. P value is not significant. There is no significant relationship between gender and occurrence of seizures. Figure 1 explains the distribution of gender in two groups from the total study sample.

Age

The Mean $\pm$ SD of age of the total study population was found to be 28.35 ± 11.7 years. Then, the patients were categorized based on their age. Out of 100 patients, 31 (31%) of them were from each of the 15-19 years & 20-29 years age group, followed by 18 (18%) from 30-39 years, 14 (14%) from 40-49 years, and 5 (5%) from 50-59 years. Only 1 (1%) participant was from the 60-69 years age group. In the present study, except in the 40-49 years and 50-59 years age group, males were found to be more in all the age groups. P value is significant. There is a significant relationship between age and occurrence of seizures. Table 1 explains about the detailed distribution of subjects with their respective age groups.

Distribution based on the type of seizures

Study participants were categorized based on the

Table 4: Dual drug therapy pattern of AED's prescription

Drugs Prescribed	No. Sub (N=35)	%
CLO+D	6	17.2
CLO+P	7	20.0
CLO+L	2	5.72
CLO+C	2	5.7
CLO+O	1	2.8
PB+D	4	11.4
PB+P	1	2.8
PB+C	1	2.8
C+L	1	2.8
C+D	2	5.7
C+P	1	2.8
D+L	2	5.7
D+P	1	2.8
D+CN	1	2.8
O+T	1	2.8
O+L	2	5.7
Total	35	100

Table 5: Triple drug therapy pattern of AED's prescription

Drugs Prescribed	No. Sub (N=17)	%
CLO+C+P	4	23.5
CLO+O+L	1	5.9
CLO+C+T	1	5.9
CLO+PB+C	2	11.7
CLO+PB+D	2	11.7
CLO+C+D	1	5.9
P+O+L	1	5.9
CLO+C+L	1	5.9
CLO+PB+O	2	11.7
PB+C+L	1	5.9
PB+C+P	1	5.9
Total	17	100

Table 6: Quadruple drug therapy pattern of AED's prescription

Drugs Prescribed	No. Sub (N=3)	%
CLO+C+D+P	1	33.3
CLO+PB+C+D	1	33.3
CLO+C+P+L	1	33.3
Total	3	100

Table 7: Drug compliance among the study participants

Age Group	High	Medium	Low	Total	P value
15-19	14	9	8	31	
20-29	12	12	7	31	
30-39	10	3	5	18	0.6483
40-49	6	4	4	14	
50-59	2	1	2	5	
60-69	1	0	0	1	
Total	45	29	26	100	

type of seizures they were diagnosed with. Out of the 100 patients, 57 (57%) were classified as GTCS, followed by 17 (17%) focal seizures, 14 (14%) CPS and the remaining 12 (12%) were classified as other types of seizures. Figure 2 explains about the detailed distribution of subjects seizures based on types among the total study population.

Distribution based on the type of classification of drugs used

In the present study, drugs belonging to Iminostilbenes were the most prescribed among the AEDs, 44 subjects (24.2%) were prescribed these drugs. This was followed by Benzodiazepines- which were prescribed to 38 subjects (20.9%),34 subjects (18.7%) were treated with Aliphatic Carboxylic acids, Hydantoins- prescribed to 25 subjects (13.7%), and newer drugs- prescribed to 24 subjects (13.2%). Barbiturates were the least prescribed among AEDs with 17 subjects (9.3%) being prescribed for this. Figure 3 explains the distribution based on type of classification of drugs used among study participants.

Type of Anti-Epileptic drugs (AEDs)

In the present study, out of the 100 sample, few participants were under poly drug therapy, i.e., more than one drug prescribed for their condition. In this manner, a total of 182 AEDs were being taken by the participants. It was found that, of these 182 AEDs, the most commonly prescribed drugs were: those treated with Clobazam were 36(20%), followed by Divalproex Sodium- 34(19%), Carbamazepine- 32(18%), Phenytoin- 25(14%), Leviteracetam- 22(12%), Phenobarbitone- 17(9%), Oxcarbazepine- 12(7%), and lastly, those treated with Topiramate and Clonazepam were only 2(1%) each. Figure 4 explains the type of Anti-Epileptic drugs used among the study participants.

Types of Prescribed Therapy

In the present study subjects we categorized and treated with different types of therapies such as 44 were Single drug therapy and followed by 35 were Double drug therapy, 17 were Triple drug therapy, 3 of them Quadrant therapy and finally 1 subject treated with five drug therapy. Table 2 explains the type of Anti-Epileptic drugs used among the study participants.

Single drug therapy pattern of AED's prescription

In the present study subjects treated with Single therapy was Prescribed to 44 subjects out of them 12(27%) are treated with Divalproex Sodium, 11(25%) are treated with Carbamazepine, 9(20%) are treated with Leviteracetam, 7(16%) are treated with Phenytoin, 4(9%) are treated with Oxcarbamazepine, and finally 1(2%) are treated with Phenobarbitone. Table 3 explains the single drug therapy pattern of AED's prescription among the study participants.

Dual Drug Therapy pattern of AED's prescription

In the present study, the dual therapy was prescribed to 35 subjects out of them the most commonly prescribed combinations are CLO+P given to 7 subjects (2 0%), followed by CLO+D given to 6 subjects (17%), followed by CLO+O given to 4 subjects (11%), followed by CLO+L,CLO+C,C+D,O+L,D+L are given to 2 subjects (6%) respectively, and finally CLO+O,PB+C,C+L,C+P,D+P,D+CN,O+T are given to 1 subject (3%) respectively. Table 4 explains the dual drug therapy pattern of AED's prescription among the study participants.

Triple Drug Therapy pattern of AED's prescription

In the present study the Triple therapy was prescribed to 17 subjects out of them the most commonly prescribed combinations are CLO+C+P are given to 4 subjects (24%), followed by CLO+PB+C,CLO+PB+D,CLO+PB+O are given to 2 subjects (12%) respectively, and finally CLO+O+L, CLO+C+T, CLO+C+D, P+O+L, CLO+C+L, PB+C+L, PB+C+P are given to 1 subject (6%) respectively. Table 5 explains the triple drug therapy pattern of AED's prescription among the study participants.

Table 8: Drug therapy in relation to the diagnosis among the study participants

Sl. No	Type of seizure	Drugs prescribed	No. of sub-jects	Type of therapy
1		C	4	Monotherapy
		P	5	Monotherapy
	GTCS	D	8	Monotherapy
		O	3	Monotherapy
		PB	1	Monotherapy
		L	6	Monotherapy
		CLO+D	4	Polytherapy
		CLO+P	7	Polytherapy
		PB+D	2	Polytherapy
		C+L	1	Polytherapy
		D+L	2	Polytherapy
		CLO+L	1	Polytherapy
		CLO+C	2	Polytherapy
		PB+P	1	Polytherapy
		D+P	1	Polytherapy
		C+D	1	Polytherapy
		C+P	1	Polytherapy
		CLO+C+P	1	Polytherapy
		CLO+O+L	1	Polytherapy
		CLO+C+T	1	Polytherapy
		CLO+PB+C	1	Polytherapy
		CLO+PB+D	1	Polytherapy
		CLO+C+D	1	Polytherapy
		CLO+C+D+P	1	Polytherapy
2		C	3	Monotherapy
	FOCAL	P	1	Monotherapy
		O	1	Monotherapy
		PB+D	1	Polytherapy
		D+CN	1	Polytherapy
		PB+C	1	Polytherapy
		O+T	1	Polytherapy
		P+O+L	1	Polytherapy
		CLO+PB+C	1	Polytherapy
		CLO+C+P	1	Polytherapy
		CLO+C+L	1	Polytherapy
		CLO+PB+D+L+CN	1	Polytherapy

Continued on next page

Table 8 continued

Sl. No	Type of seizure	Drugs prescribed	No. of subjects	Type of therapy
3		D	2	Monotherapy
		C	3	Monotherapy
		L	1	Monotherapy
		PB+D	1	Polytherapy
		O+L	1	Polytherapy
		CLO+O	1	Polytherapy
		CLO+L	1	Polytherapy
		CLO+D	1	Polytherapy
		PB+C+L	1	Polytherapy
		CLO+PB+O	2	Polytherapy
		PB+C+P	1	Polytherapy
		CLO+C+P	1	Polytherapy
		CLO+PB+D	1	Polytherapy
4		D	2	Monotherapy
		C	1	Monotherapy
		L	2	Monotherapy
		P	1	Monotherapy
	OTHERS	CLO+D	1	Polytherapy
		O+L	1	Polytherapy
		C+D	1	Polytherapy
		CLO+C+P	1	Polytherapy
		CLO+PB+C+D	1	Polytherapy
		CLO+C+P+L	1	Polytherapy

Quadruple drug therapy pattern of AED's prescription

In the present study, the Quadruple therapy was prescribed to 3 subjects out of them the most commonly prescribed combination is CLO+C+D+P,CLO+PB+C+D,CLO+C+P+L are given to 1 subject (33.33%) respectively. Table 6 explains the Quadruple drug therapy pattern of AED's prescription among the study participants.

Quintuple drug therapy pattern of AED's prescription

In the present study, CLO+PB+D+L+CN was the five drug combination and given to a single subject.

Drug Compliance

In the present study, overall drug compliance was found to be better as the participants with high level of drug compliance were 45 (45%), and those with low level of drug compliance were 26 (26%). p value is not significant. There is no significant relationship between age and drug compliance. But when compared with number of seizure attacks past 3 months, p value is significant. There is a significant relationship between number of seizure attacks past 3 months and drug compliance. Table 7 explains the Drug compliance among the study participants.

Drug therapy in relation to the diagnosis

In the present study, type of drug therapy varied with the diagnosis among the study participants. The results are presented in Table 8.

Prescribing of newer vs older antiepileptics

In the present study, older antiepileptic drugs were most prescribed than newer antiepileptic drugs. Results are depicted in Figure 5.

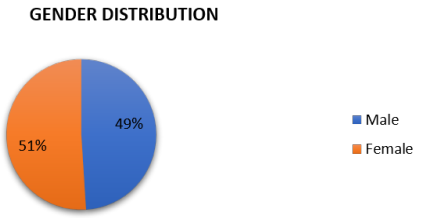

Figure 1: Gender wise distribution of the study participants

DISCUSSION

Gender

Among 100 patients studied; we seen female (N=51, 51%) were predominant than males (N=49, 49%). In contrast to our results; Murthy NV et al. [18], showed males were more frequently attacked with

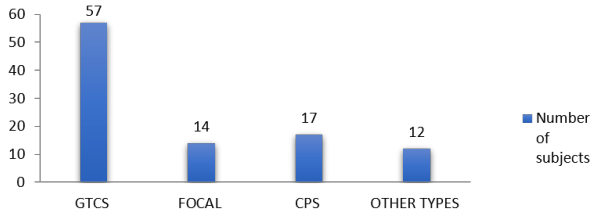

Figure 2: Type of seizure distribution among the study participants

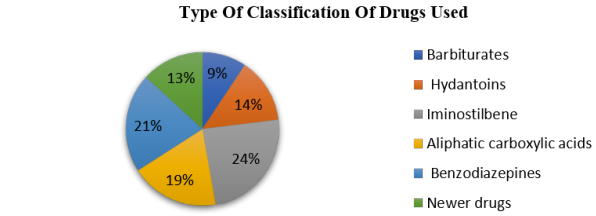

Figure 3: Distribution based on type of classification of drugs used

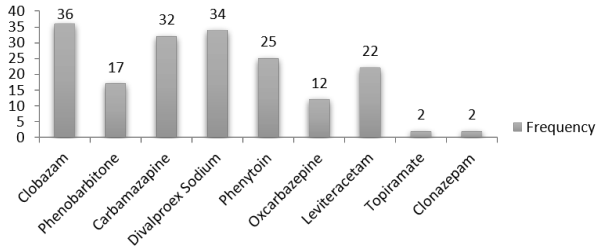

Figure 4: Type of Anti-Epileptic drugs used among the study participants

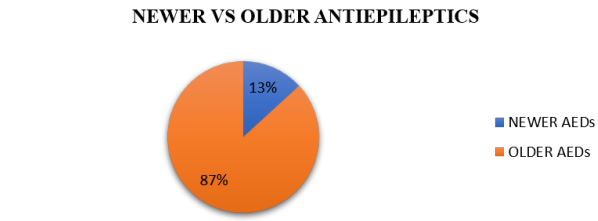

Figure 5: Prescribing of Newer Vs Older Antiepileptics among the Study Population

epilepsy than females. It is however that T.Badwaik et al. [4], seen females were more than males in their study exposed to antiepileptic drugs, which complements our result.

Age

The average age of the patients in the present study was 28.35±11.7 years. In the present study, both age groups of 15-19 and 20-29 has highest percentage of patients, with each group having 31(31%) patients. The age groups in descending order contains followed by 18 (18%) from 30-39 years, 14 (14%) from 40-49 years, 5 (5%) from 50-59 years,

and finally the least number of patients i.e., 1 (1%) from 60-69 years. The results are similar to the studies from Faizan Mazhar et al. [4], Nurulumi Ahmad et al. [22] and Kavitha Palanisamy et al. [23].

All the above studies concluded that most of the epileptic patients were from the age groups of 10-30. In Faizan Mazhar et al. [4]. 24.75 % of patients being younger than 19 years of age. In Nurulumi Ahmad et al. [22], there were 24 (46.2%) patients under the age of 30 years, 22 (42.3%) patients between 30-60 years and 6 (11.5%) patients above 60 years. In Kavitha Palanisamy et al. [23], patients between age group 0-14 years were dominant with 59 (32.78%) subjects followed by patients from the age group 15-29 years (25.55%). From this it is clearly evident that adults are more likely to have epilepsy than any other age group.

Types of Epilepsy

In our hospital, most patients were suffering from generalized tonic clonic seizures, followed by Complex partial seizures, Focal seizures, and other types of seizures. A study from Mysore, South India also seen similar pattern of epilepsy [19]. These results are similar to the studies conducted by Kavitha Palanisamy et al. [23], Ramesh Rajesh Pol et al. [24], where they concluded that generalized tonic clonic seizures are the most frequent type to occur among all types of seizures. In Kavitha Palanisamy et al. [23], majority of the study subjects were affected with generalized seizures and 84 (46.66%) subjects had generalized tonic clonic seizure followed by 35 (19.44%) cases of complex partial seizures and 28 (15.55%) cases of myoclonic seizures. Whereas, in Ramesh Rajesh Pol et al. [24] occurrence of seizures depicts a highest percentage of generalized seizures (51%) than the partial and other types.

Type of prescribed therapy

Problems in polytherapy is undue increase in cost, drug interaction with other drugs, increased chance of side effects and less compliance to patient which can be complicating the therapy leading to decrease in therapeutic outcome. Careful administration of other antiepileptic is needed if necessary.

In the present study, it is observed 44 patients were on single drug therapy(45%), 35 were on double drug therapy (35%), 17 were on triple drug therapy (17%), 3 patients were treated with four drugs (3%) and finally 1 patient was treated with five drug therapy. These results are in concordance with studies done by Murthy VN et al. [18], Arulkumaran KSG et al. [25], Malerba A. et al. [26], where they found that most of the patients were prescribed single drug. These results are also similar to the study Shilpa B. N. et al. [27], where majority of patients received monotherapy with various drugs (67%). About 33% of the patients received combination therapy with two or more drugs. Guidelines mention that medical management of newly diagnosed epileptic patients should start with monotherapy. Polytherapy should be considered when failure of two attempts of monotherapy.

Type of AEDs among study population

There are above 20 antiepileptic drugs which are available for clinical use today. In the present study, 9 different antiepileptic drugs were used. However. In 100 prescriptions a total of 182 antiepileptic drugs were used. , Clobazam 36(i.e., 20%) is the most prescribed drug followed by divalproex sodium 34(19%) and carbamazepine 32(18%). This study highlighted that clobazam was the most commonly prescribed antiepileptic drug. Recently published studies (2002- 2013), Pathak S et al. [28], Malerba A et al. [26], Landmark CJ et al. [29], mention that divalproex sodium was the most commonly drug prescribed followed by phenytoin or other drugs. An Indian study by Thomas SV et al. [30], in 2001 mentioned that carbamazepine was prescribed most commonly. In the present study newer drugs such as Topiramate and clonazepam were not used frequently. This illustrates the existence of wide variation in prescribing the antiepileptic drugs. The reason for discrepancies may be attributed to factors like availability, affordability, place of practice, type of epilepsy and preference of treating neurologist. Clobazam is an antiepileptic belonging to benzodiazepines most commonly used for complex partial onset seizure as well as generalised tonic clonic seizures in combinations. Being cheap, it is also widely available, which enhances its use in our set up of tertiary care hospital.

Indication wise use of Antiepileptic drugs

Drug therapy is the mainstay of epilepsy treatment. The choice of antiepileptic drugs will depend on type of epilepsy, drug specific adverse drug reactions and patient preferences. To treat epilepsy, basic treatment approach is to begin with monotherapy, where about 50% to 70% of patients can be maintained on one antiepileptic drug. Among 57 Generalised tonic clonic seizures patients single drug was prescribed to 27 patients, 23 patients were prescribed two drugs and remaining 7 patients were prescribed with more than 2 drugs. From the present study it is observed that it is observed divalproex sodium is the most commonly used drug in single drug prescribed patients followed by leviteracetam to patients suffering with generalized tonic-clonic seizures. In poly therapy receiving

patients Clobazam along with the phenytoin is the most commonly prescribed combination followed by Clobazam along with divalproex sodium.

Among 14 focal Seizure patients, single drug was prescribed to 5 patients, 4 patients were prescribed two drugs and remaining 5 patients were prescribed with more than 2 drugs. It is observed carbamazepine is the most commonly prescribed drug to the focal seizures patients as monotherpy. Whereas, Clobazam is the most commonly prescribed drug along with add-ons such as Phenobarbitone, carbamazepine, and in 1 case phenytoin along with Clobazam and leviteracetam along with Clobazam is also used.

Among 17 Complex Partial Seizure patients single drug was prescribed to 5 patients, 4 patients were prescribed two drug regimen and remaining 5 patients were prescribed with more than 2 drugs. In this study we observed that it is observed carbamazepine is the most commonly prescribed drug to patients suffering with complex partial seizures receiving single drug. Similar results were found in Shobhana Mathur et al. [31]. Whereas, in patients receiving two drugs clobazam is commonly used drug. It is used in combination with drugs such as carbamazepine, leviteracetam, and divalproex sodium. In patients receiving more than two drugs, clobazam is frequently used combined with phenobarbitone and oxcarbazepine. Among 12 other types of Seizure patients single drug was prescribed to 6 patients and 3 patients were prescribed two drugs and remaining 3 patients were prescribed with more than 2 drugs. From this study, it is observed that in other types of seizures divalproex sodium and leviteracetam are the drugs commonly used in patients receiving single drug. Whereas in patients receiving two drugs divalproex is mainly used drug with combination of either clobazam or carbamazepine. In patients receiving more than 2 drugs clobazam is commonly used along with carbamazepine and phenytoin. Based on these findings we highlighted that divalproex sodium is the drug mainly used in generalised tonic clonic seizures, complex partial seizures, and other types of seizures as monotherapy. Leviteracetam is the drug mainly used in generalised tonic clonic seizures, and other types of seizures as monotherapy. Whereas carbamazepine is used in focal seizures and complex partial seizures as monotherapy. Clobazam is the main drug used in any type of seizures in combination with other antiepileptics.

Single therapy

In the present study single drug therapy was prescribed to 44 subjects. From the results of the study, it is observed that divalproex sodium is the most commonly used drug given to 12 (27%) patients followed by carbamazepine, leviteracetam, phenytoin oxcarbazepine and lastly phenobarbitone which were given to 11 (25%), 9 (20%), 7 (16%), 4 (9%) and 1 (2%) of the patients as a monotherapy respectively.

In a study done by Meenakshi B et al. [32], Divalproex sodium was the most commonly used monotherapeutic agent followed by carbamazepine, leviteracetam, phenytoin and lastly phenobarbitone. So, the present study is in concordance with study done by Meenakshi B et al.

Dual therapy

In the present study dual drug therapy was prescribed to 35 patients. Upon considering the results of the study it is observed that the most commonly prescribed combination is clobazam along with phenytoin which constitutes 20% (7) of the patients receiving dual drug therapy. Followed by clobazam along with Divalproex sodium constitutes 17%(6), clobazam along with oxcarbazepine 11%(4).

Combination of Clobazam with either leviteracetam or carbamazepine constitutes 6% of the patients receiving the dual drug therapy.

The similar study was conducted by Meenakshi B et al. [32], where they found that the most commonly prescribed combination was divalproex sodium with carbamazepine followed by divalproex sodium with phenobarbitone. When the present study compared to this there is no similarity between them. From the present study, Clobazam is the most commonly prescribed drug in combination therapy.

Ngangom Gunindro et al. [14], concluded that Oxcarbazepine with Clobazam was the most prescribed 2 drugs combination (36%) while Oxcarbazepine.

Triple therapy

In the present study triple drug therapy was prescribed to 17 subjects. From the results of the study, it is observed that the most prescribed combination is clobazam +carbamazepine+ phenytoin which constitutes 24% (4) of the patients receiving triple drug therapy. Followed by combination of clobazam and phenobarbitone with Carbamazepine, divalproex sodium, oxcarbazepine constitutes the second most portion of the patients receiving triple drug therapy with 12% each. Finally combinations of clobazam with other antiepileptics occupy the next place among patients with triple drug therapy.

The similar study was conducted by Meenakshi B et al. [32], where they found that the most

commonly prescribed combination was divalproex Sodium with phenytoin and carbamazepine. When the present study compared to this there is no similarity between them. From the present study, Clobazam is the most commonly prescribed drug in combination therapy.

Ngangom Gunindro et al. [14], concluded that Clobazam with Levetiracetam topped the list of 3 drugs combinations.

Quadruple therapy

In the present study, Quadruple drug therapy was prescribed to 3 subjects. From the results of the study it is observed that the most prescribed combination is clobazam + carbamazepine +divalproex sodium +phenytoin and clobazam+phenobarbitone+carbamazepine +divalproex sodium and clobazam + carbamazepine +phenytoin +leviteracetam are the three types of combinations prescribed to each patient constituting 33.3%.

The similar study was conducted by Ngangom Gunindro et al. [14], where they found that 33.33% of the 4 drugs combinations comprised of Oxcarbazepine, Phenobarbitone, Levetiracetam and Divalproex combination.

Quintuple therapy

In the present study, quintuple therapy was prescribed to one patient. The combination of Clobazam + Phenobarbitone + Divalproex sodium + Leviteracetam + Clonazepam was prescribed. No other studies mentioned about quintuple therapy.

Type of Classification of AEDs Prescribed

In the present study, six groups of antiepileptic agents were prescribed to the epileptic patients. Among them Iminostilbenes were the most commonly prescribed, which constitutes (24%) given in 44 prescriptions. Benzodiazepines were prescribed in 20.879% followed by aliphatic carboxylic acids which were prescribed to 18.681%. Hydantoins were prescribed to 13.736%, Newer drugs were prescribed 13.187% and lastly Barbiturates were the least prescribed group among AEDs accounting for 17 prescriptions 9.3407%.

Prescribing of newer VS older Antiepileptics

Drugs introduced before and 1990's are called older and newer antiepileptic drugs respectively. In the present study, it is observed that It is observed newer antiepileptic drugs were prescribed very rarely when compared to older ones. This is similar to Arulkumaran KSG et al. [25], study performed in India, which highlighted the limited use of newer antiepileptics drugs. Guidelines for the management of epilepsy in India, 2013 shows that newer antiepileptic drugs and their discovery has not altered treatment regimen. However, it has increased treatment choice in refractory cases. So far, no study has shown that newer drugs have superior anticonvulsant efficacy than older ones. Less usage in our settings may also be due to higher cost of these agents compared to older ones. In present study the present study it is observed that it is observed Leviteracetam, Clonazepam, Topiramate, oxcarbazepine are the frequently used newer antiepileptic drugs and Carbamazepine, Phenytoin, divalproex sodium, Clobazam and Phenobarbitone are the older ones that are prescribed. Two drug combination is far more common than the triple and quadruple anti-epileptic regimens.

Medication Adherence

Adherence to medication is defined as the extent to which a patient's behavior taking the medication prescribed by the physician changes after therapeutic plan agreement is established, between patient and physician [33]. Adherence level of the patient is relied upon on the drug side effects, which can be easily resolved. In epilepsy, patients have to take medications for years. Hence, observing medication adherence behavior of this patient vital. Medication adherence can be assessed by indirect or direct methods. Direct observed therapy, measurement of the level of medication or metabolite and biological markers in the blood are direct methods to observe medication adherence. Indirect methods include patient self-reporting, records of drug refills, pill counts, patient's treatment response assessment and the use of electronic medication-monitoring devices. In the present study patient self-reporting method is used to assess medication adherence by validated MMAS-8 questionnaires. This questionnaire consists of 8questions where 0 is given to answer 'Yes' and 1 is given to answer 'No' from question 1 to 7where as in question number 8, answer are reported in 0 to 4 scale. After filling the questionnaire one can add all the score to provide medication adherence score for patient which can come from 0 to 8. Further these score are classified as adherence level as high adherence (0), medium adherence (1-2) and low adherence (3-8).

In the present study it is observed that 45% of the patients were having it is observed high medication adherence 45 %, 29% of patients having medium adherence and finally low medication adherence in 26% patients.

CONCLUSION

Based on the results we would like to conclude that: Females were predominant than males. Adults were more prone to epilepsy. Generalised tonic clonic seizures were the most common type of seizures occurring followed by Complex partial seizures. Iminostilbenes were the most prescribed classification of antiepileptic drugs followed by Benzodiazepines and Aliphatic carboxylic acids. The average number of antiepileptic drugs prescribed per patient was approximately 2 drugs. Clobazam was the most prescribed drug among study population. Single drug therapy was the most common type of therapy prescribed followed by Double drug therapy, and Triple drug therapy. In single drug therapy, Divalproex sodium, in dual therapy clobazam along with phenytoin and in triple therapy combination of clobazam, carbamazepine, phenytoin were mostly prescribed. There was high medication adherence among study patients followed by medium and low medication adherence. Drug therapy was specific to respective indications. Very less new antiepileptic drugs were used than older ones in prescriptions.

ACKNOWLEDGEMENT

We thank to Dr. Venugopal sir, MBBS, MD General Medicine, DM Neurology, who supported us in our study.

Ethical Considerations

We obtained patient informed consent and done our study in the guidance of health experts without harm to the subjects.

Conflict of Interest

The authors declare that they have no conflict of interest.

Funding Support

The authors declare that they have no funding support for this study.

REFERENCES

[1] Stuart H Ralston, Ian D Penman, Mark W J Strachan, and Richard P Hobson. Davidson's Principles and Practice of Medicine. pages 1167–1169, 2018. 23rd Edition.

[2] Roger Walker and Cate Whittlesea. Clinical Pharmacy and Therapeutics. pages 447–448, 2007. Fourth Edition .

[3] Joseph T Dipiro, Robert L Talbert, Robert L Dipiro, Gary C Talbert, Gary C Yee, Gary C Matzke, Barbara G Wells, and L Michael Posey. Pharmacotherapy: A Pathophysiologic Approach. page 927, 2008. Seventh Edition, Chapter-58.

[4] Alan H Mutnick, Paul F Souney, Larry N Swanson, and Leon Shargel. Comprehensive Pharmacy Review . pages 746–748, 2012. Eighth Edition.

[5] Epilepsy Foundation and Epilepsy Together. What is Epilepsy?, 2019. Accessed on: 25 Apr 2021.

[6] Senthil Amudhan, Gopalkrishna Gururaj, and Parthasarathy Satishchandra. Epilepsy in India I: Epidemiology and public health. *Ann Indian Acad Neurol*, 18(2):263–277, 2015.

[7] Epilepsy Foundation and Epilepsy Together. Types of Seizures, 2017. Accessed on: 25Apr 2021.

[8] G D Hammer and S J McPhee. Pathophysiology of disease: an introduction to clinical medicine. New York, 2010. McGraw-Hill Medical. New York: McGraw-Hill Medical, ISBN: 978-0-07-162167-0.

[9] E B Bromfield. An Introduction to Epilepsy. *American Epilepsy Society*, 2006.

[10] Hal Blumenfeld. Cellular and Network Mechanisms of Spike-Wave Seizures. *Epilepsia*, 46(s9):21–33, 2005.

[11] Amna Rana and Alberto E. Musto. The role of inflammation in the development of epilepsy. *Journal of Neuroinflammation*, 15(1), 2018.

[12] J L Noebels and M Avoli. Jasper's Basic Mechanisms of the Epilepsies. pages 466–470. Oxford University Press, ISBN: 9780199746545.

[13] Michel Le Van Quyen, Vincent Navarro, Jacques Martinerie, Michel Baulac, and Francisco J. Varela. Toward a Neurodynamical Understanding of Ictogenesis. *Epilepsia*, 44(s12):30–43, 2003.

[14] Fernando Lopes da Silva, Wouter Blanes, Stiliyan N. Kalitzin, Jaime Parra, Piotr Suffczynski, and Demetrios N. Velis. Epilepsies as Dynamical Diseases of Brain Systems: Basic Models of the Transition Between Normal and Epileptic Activity. *Epilepsia*, 44(s12):72–83, 2003.

[15] Ethan M. Goldberg and Douglas A. Coulter. Mechanisms of epileptogenesis: a convergence on neural circuit dysfunction. *Nature Reviews Neuroscience*, 14(5):337–349, 2013.

[16] National Clinical Guideline Centre. The Epilepsies: The diagnosis and management of the epilepsies in adults and children in primary

and secondary care (PDF), 2012. National Institute for Health and Clinical Excellence. pp. 21–28. Archived (PDF) from the original on 16 December 2013, Accessed on: 25 Apr 2021.

[17] National Clinical Guideline Centre. The Epilepsies: The diagnosis and management of the epilepsies in adults and children in primary and secondary care (PDF), 2012. National Institute for Health and Clinical Excellence. pp. 119–129. Archived (PDF) from the original on 16 December 2013, Accessed on: 25 Apr 2021.

[18] Emily Oby and Damir Janigro. The Blood?Brain Barrier and Epilepsy. *Epilepsia*, 47(11):1761–1774, 2006.

[19] G G Somjen. Ions in the Brain Normal Function, Seizures, and Stroke. page 167, 2004. New York: Oxford University Press, ISBN: 978-0-19-803459-9.

[20] J Engel and T A Pedley. Epilepsy: a comprehensive textbook. page 483, Philadelphia. (2nd ed.). Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins, ISBN 978-0-7817-5777-5.

[21] Barbara G Wells, Terry L Schwinghammer, Patrick M Malone, Jill M Kolesar, John C Rotschafer, T Joseph Dipiro, and Marie A. Chisholm-Burns. Pharmacotherapy Principles and Practice. pages 447–448, 2007.

[22] Nurulumi Ahmad, Nurul Izaty Othaman, and Farida Islahudin. Medication Adherence And Quality Of Life In Epilepsy Patients. *Int J Pharm Pharm Sci*, 5(Suppl 2):401–404, 2013.

[23] Keerthy Jayalakshmi, Kavitha Palaniswamy, Sambathkumar Ramanathan, and Sruthi Akela. A Study on the Adverse Drug Reactions Induced by Anti Epileptic Drugs in the Epileptic Patients. *Journal of Applied Pharmaceutical Science*, 6(05):119–123, 2016.

[24] Jincy George, Julia Jose, Divya Ashok Kulkarni, Ramesh Rajesh Pol, Mallappa Hanamantappa Shalavadi, and Chandrashekhar Venkaraddi Mangannavar. Evaluation of Drug Utilization and Analysis of Anti- Epileptic Drugs at Tertiary Care Teaching Hospital. *Indian Journal of Pharmacy Practice*, 9, 2016.

[25] C L Harden, J Hopp, T Y Ting, et al. Management issues for women with epilepsy-Focus on pregnancy (an evidence-based review): I. Obstetrical complications and change in seizure frequency: Report of the Quality Standards Subcommittee and Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology and the American Epilepsy Society. *Epilepsia*, 50(5):1229–1236, 2009.

[26] A Malerba et al. Patterns of prescription of antiepileptic drugs in patients with refractory epilepsy at tertiary referral centres in Italy. *Epilepsy research*, 91(2-3):273–282, 2011.

[27] B N Shilpa, H K Sushma, S Latha, and G H Shashikala. Prescription pattern of antiepileptic medications in a tertiary care centre. *Indian Journal of Pharmacy and Pharmacology*, 5(1):7–10, 2018.

[28] Sachchidanand Pathak, Lalit Singh, Tanuja Singh, and S K Sharma. Prescribing patterns of Anti-epileptic drug in different age group in India. *Journal of Drug Discovery and Therapeutics*, 2013(1):69–75.

[29] Cecilie Johannessen Landmark, Hilde Fossmark, Pål G. Larsson, Elisif Rytter, and Svein I. Johannessen. Prescription patterns of antiepileptic drugs in patients with epilepsy in a nation-wide population. *Epilepsy Research*, 95(1-2):51–59, 2011.

[30] S. V. Thomas, P. S. Sarma, M. Alexander, L. Pandit, L. Shekhar, C. Trivedi, and B. Vengamma. Economic Burden of Epilepsy in India. *Epilepsia*, 42(8):1052–1060, 2001.

[31] Shobhana Mathur, Sumana Sen, L Ramesh, and M Satish Kumar. Utilization Pattern of Antiepileptic Drugs and their Adverse Effects in a Teaching Hospital . *Asian Journal of Pharmaceutical and Clinical Research*, 3(1), 2010.

[32] B Meenakshi, J Ezhil Ramya, and T R R Ananthy Shri. An analysis of prescription pattern and adverse drug reaction profile in children treated with antiepileptic drugs in a tertiary care teaching hospital. *Int J Basic Clin Pharmacol*, 5(2):389–393, 2016.

[33] Lars Osterberg and Terrence Blaschke. Adherence to Medication. *New England Journal of Medicine*, 353(5):487–497, 2005.

Copyright: This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

Cite this article: Dinesh Kumar Kukunuri, Richard Noah, Sugreev Dwivedi Anuj, Sasi Karnati. Prescribing Patterns of Anticonvulsant Drugs in Epilepsy in a Tertiary care Hospital: An Observational Prospective Study. Int. J. of Clin. Pharm. Med. Sci. 2021; 1(2): 54-69.

© 2021 Pharma Springs Publication.