"A STUDY ON DRUG UTILIZATION PATTERN OF ANTIEPILEPTIC DRUGS IN RURAL TERTIARY CARE TEACHING HOSPITAL"

BY

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Under the Guidance of

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DEDICATED TO MY FATHER AND MOTHER

JEER.SURESH

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ABBREVIATIONS

AH & RC	Adichunchanagiri Hospital And Research Centre
AIMS	Adichunchanagiri Institute Of Medical Science
ADR	Adverse Drug Reaction
AED	Antiepileptic Drug
GTCS	Generalized Tonic-Clonic Seizure
DDI	Drug-Drug Interaction
WHO	World Health Organization
U.K	United Kingdom
U.S.	United State
PHT	Phenytoin
LEV	Levetiracetam
CBZ	Corbamazepine
PB	Phenobarbitone
PB	Drug Utilization Review
VPA	Valproate
DUE	Drug Use Evaluation
ASHP	American Society Of Health System Pharmacists
MUE	Medication Use Evaluation
MMAS	Morisky Medication Adherence Scale

Abstract

ABSTRACT

BACKGROUND:

There is evidence of different patterns of drug utilisation of antiepileptic drugs in our country. Newer drugs are becoming available now and how these drugs are utilised is very interesting to see. Problems in antiepileptic therapy like use of polytherapy, adverse drug reactions, drug interactions, lack of adherence to medications etc., can be identified and resolved by clinical pharmacist. Considering all these facts we started study with title "A study on drug utilization pattern of antiepileptic drugs in rural tertiary care teaching hospital"

MATERIALS AND METHODS:

Prospective observational study of 9 months duration from July 2015 to February 2016 was carried out after human ethics research committee approval. All in-patients prescribed with anti-epileptic drugs in Paediatric & General medicine department were selected. Data were collected in customized data collection form after taking patient consent and also from patient case sheets/prescriptions. Morisky Medication Adherence Scale-8 questionnaire was used to assess the adherence at baseline. Data were measured in percentage and frequency using descriptive statistics. Microsoft excel was used to summarize the analysis of data.

RESULTS:

A total of 120 patients enrolled to study where 209 antiepileptic drugs were prescribed. Females (58%) and patients with age group of 0-18 years (58.33%) were more exposed to these drugs. 80% of diagnosis was epilepsy without any co-morbidity. Prescription pattern of drugs showed that Phenytoin (34.44%) was the most common drug used either as single or in combination with other drugs to treat several of indication. At maximum 4 antiepileptic drugs were seen in one prescription introducing polytherapy (64.16%). We seen very less (3.82%) prescriptions for newer compared to older generation antiepileptiics. Among total 82(68.3%)

drug interactions which were identified, 43.9% were severe, 39.02% were mild and 17.073% were moderate ones. We also seen 66.66% of patient were having poor medication adherence score at baseline. We counselled these patients. All interventions were accepted by physician.

CONCLUSION: Very less new antiepileptic drugs were used with high evidence of polyptherapy. Phenytoin was the most commonly prescribed drug. Clinical pharmacist mediated services helped to identify and reduce drug therapy related problems.

KEY WORDS: Antiepileptics drug, prescribing pattern, polytherapy, drug interaction.

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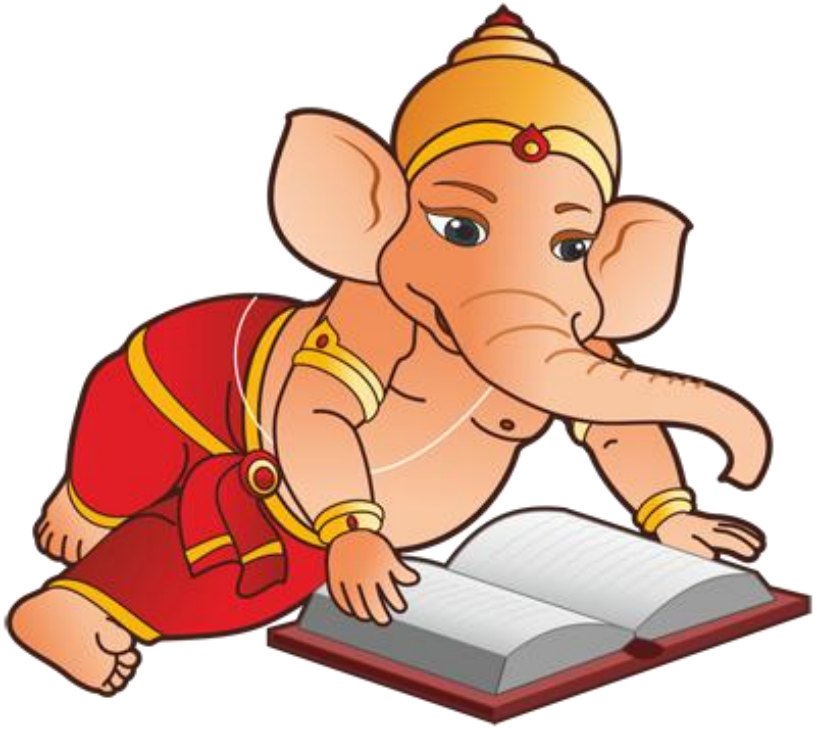


Introduction

INTRODUCTION

Drug utilization is defined by World Health Organization (WHO) as the study of marketing, distribution, prescription and use of drugs in a society, with special emphasis on the resulting medical, social and economic consequences. Drug utilization research helps in identification of clinical use of drugs in populations and its impact on healthcare system.[1]

The aim of drug utilization study is to improve rational use of drugs in populations. For the individual patient, rational use of a drug implies the prescription of a well-documented drug in an optimal dose on the right indication, with the proper information and at a low-cost price. Without knowledge on how drugs are being prescribed and used, it is difficult to initiate a decision on rational drug use and to suggest measures to change prescribing habits for the better. Information on the past performance of prescribers is the essential of any auditing system. Drug utilization study in itself does not necessarily provide answers, but it contributes to rational drug use.[2] Continued clinical usage for many decades, some head to head randomized double blind trails, many open label randomized trials and post marketing trials have represents the profiles of traditional antiepileptic drugs (AEDs). So there is need to perform drug utilization studies.[3]

Epilepsy is the most common neurological condition worldwide with Indian prevalence of 572.8/100,000 population/year. This shows rising trends as treatment gaps for active epilepsy exceeded 75% in most low-income countries. Peoples may expose to different antiepileptics. So there may be differing trend of utilization of antiepileptics.[4]

The mainstay of management of epilepsy is antiepileptics.[5] There are two different types of antiepileptics i.e. older and newer generation. The older (traditional) AEDs included Phenobarbital, Phenytoin, Primidone, Ethosuximide, Benzodiazepines, Carbamazepine and Valproate, while the newer AEDs has the list of Felbamate, Gabapentin, Lamotrigine, Pregabalin

etc.[6] New AEDs have been marketed during the last 20 years. There is still a lack of documentation of safety aspects regarding many of these drugs, as the use in special patient populations like children, women of child bearing age, and elderly. [7] Apart from epilepsy; AEDs are also used to treat multiple non-epilepsy disorders like neuropathic pain, migraine, essential tremor, spasticity, restless legs syndrome, bipolar disease, schizophrenia, and anxiety disorders in which both classic and newer AEDs may be used. Correspondingly, in traumatic brain injury, Parkinson's or Alzheimer's disease, alcohol abuse and obesity also antiepileptics are utilized.[8]

Until recently, only a limited number of anti-epileptic drugs were available and all had troublesome side effects. There have been several new AEDs launched since 1990. Newer AEDs are mainly used as additional treatment in people whose epilepsy is not well controlled on older AEDs alone. Newer AEDs are promoted as effective as older drugs but with less side effects.[9] Despite more than 20 approved antiepileptic drugs, about 30% of patients are refractory to treatment. An important characteristic of pharmacoresistant epilepsy is that most patients with refractory epilepsy are resistant to several, if not all, AEDs, even though these drugs act by different mechanisms. Pharmacoresistant epilepsy is a major health problem, associated with increased morbidity and mortality, and accounting for much of the economic burden of epileptic patients.[10]

Population-based studies of drug utilization demonstrate that 19-24 % of patients with epilepsy use polytherapy with AEDs. In recent studies of children and adults with refractory epilepsy, 64% used polytherapy with two or more AEDs, and 35% of the adults suffered from CNS-related comorbid conditions, resulting in a considerable risk of interactions. Polytherapy and the

potential for interactions with other drugs increase with increasing age, and the elderly is the largest group with new onset epilepsy having a considerable risk of interactions with commonly prescribed drugs other than epilepsy, including migraine, neuropathic pain, bipolar disorder, anxiety, and many other disorders. [11] More studies are required to evaluate their use as first line AEDs for children with epilepsy. Caution must be exercised for possible drug interactions with conventional AEDs before using them as an adjunct.[12]

Nowadays, the WHO definition of adherence has been universally accepted; the extent to which a person's behavior – taking medication, following a diet, and or executing lifestyle changes – corresponds with the agreed recommendations from a provider. This definition highlights the importance of an active involvement of the patient with the health professionals with a good communication. In developed countries, non-adherence to the treatment of chronic diseases ranges from 30% to 50%, and this rate is even higher in developingcountries.[13] Most interesting is that 60% of treated adults stop taking medication without relapse within 2-5 years of treatment. The adherence behavior of patient can be increased to effectively manage the epilepsy. [14]

A survey undertaken by Neurologists in the USA revealed that 71% of patients with Epilepsy forgot to take their AED (anti-epileptic drug) at least once per month and the chance of a patient missing a dose increased with the number of tablets prescribed. Of patients that missed a dose 45% reported a seizure. Similar results were reported in a recent UK study which revealed that 59% of epilepsy patients had poor compliance and that this was related to an increased frequency of seizures. Non-compliance significantly increases the risk of seizure, A&E visits,

hospitalization, road traffic accidents, fractures and death and is therefore key contributor to suboptimal management.[15]

Poor patient adherence to medication is one of the most common causes of increased morbidity and mortality. Lack of adherence has been estimated to cost the U.S. health care system between $100 billion and $289 billion annually in direct costs. Many studies are carried out to examine the current situation of medication adherence, its predictors, its relationship to patient outcomes and ways to improve it. Therefore, finding accurate and standardized measurements of medication adherence is of great importance.[16] Antiepileptic medication should not be prescribed without a careful evaluation of the risks and benefits of treatment and a discussion with the individual patient about the merits and potential side effects of treatment. Most patients with epilepsy will become seizure-free with appropriate antiepileptic drug (AED) treatment and will then be reviewed by primary care services.[17]

Other set of problems in anti-epileptics are: adverse drug reactions (ADRs) and drug interactions. These are major clinical problems in both paediatrics and adult medicine. Systematic reviews and meta-analyses of prospective studies of drug surveillance in children have showed that one in 10 children in hospital will experience an ADR. One in every 500 children will experience an ADR each year. There are significant ADRs in association with the newer AEDs. Additionally, the reporting of drug toxicity in clinical trials of AEDs is poor.[18]

In a recent Cohort study at 1998, the risk for "AED hypersensitivity syndrome" (AHS), which is characterized by the triad of fever, skin rash, and single or multi-organ system involvement in first-time users of PHT or CBZ was estimated at 2.3-4.5/10,000 and 14.1/10,000 patients,

respectively . However, up to 3 1 % of patients receiving AED therapy may complain of one or more ADRs, as shown in a recent multicenter survey.[19]

A study carried out in 2014, it was found that up to 61% of patients taking conventional AEDs, such as Phenytoin, Carbamazepine, Valproate and Phenobarbital may give rise to unexpected ADRs like cutaneous reaction and serious hematological disorder, central nervous system (CNS) abnormalities, or hepatic failure. Most of these disorders are related to toxic metabolic products of AEDs which are thought to contribute to initial treatment failure in up to 40% of patient [20].

Antiepileptic drugs show clinically significant interactions both with each other and with other medications, because of the specific pharmacokinetic profile and relatively narrow therapeutic range. Unpredicted changes of the patient's clinical condition with the controlled dosage are mainly caused by the occurrence of interactions.[6] There are two types of drug interactions between drugs such as pharmacokinetic and pharmacodynamic. For AEDs, pharmacokinetic interactions are the most notable type, but pharmacodynamic interactions involving reciprocal potentiation of pharmacological effects at the site of action are also important. By far the most important pharmacokinetic interactions are those involving cytochrome P450 isoenzymes in hepatic metabolism.[5] When multiple drug therapy is used, there is a possibility of clinically relevant drug interactions, which in patients with epilepsy are particularly common for a variety of reasons

1) AEDs are administered for prolonged periods, often for a lifetime, thereby increasing the probability of co prescription.
2) Most AEDs have a narrow therapeutic index, and even relatively modest alterations in their pharmacokinetics can result in loss of response or toxic effects.

3) The most widely used AEDs (carbamazepine, valproic acid, phenytoin and phenobarbital) have prominent effects on the activity of enzymes which metabolize the majority of existing medication.
4) Most of the old and new generation AEDs are substrates of the same enzymes. [21]

Developing countries have limited funds available for health care and drugs so it becomes very important to prescribe drugs rationally so that the available funds can be utilized optimally. More studies are required to evaluate their use as first line AED for children with epilepsy, caution must be exercised for possible drug interactions with conventional AEDs before using them as an adjunct. [22]

The interest in drug utilization studies began in the early 1960s and its importance has increased since then due to increase in marketing of new drugs, wide variation in the pattern of drug prescribing and consumption, growing concern about delayed adverse effects and the increasing concern regarding the cost of drugs.[23] As drug utilization studies serve as a mean to interpret, intervene and promote the rational prescribing, dispensing and administration of medication. Thus, the ultimate outcomes of DUR are: improved quality of patient care, better therapeutic outcomes and cost effective pharmacotherapy.[7]

Adichunchanagiri Hospital and Research Centre (AH&RC) is a 1050 bedded tertiary care teaching hospital situated in a rural area of B.G Nagara of Nagamangala,Taluk, Mandy District. Where there were no studies conducted previously in this rural hospital regarding the assessment of antiepileptic drugs use. Hence, the present study was undertaken to know the drug usage pattern in epileptic patients.

Objectives

OBJECTIVES OF THE STUDY

PRIMARY OBJECTIVE:

- To study the drug utilization pattern of antiepileptic drugs in rural tertiary care teaching hospital.

SECONDARY OBJECTIVES:

- To identify the common class of drugs prescribed and indication for therapy.
- To assess the adverse drug reactions of prescribed drugs.
- To assess and identify the potential drug interactions.
- To identify the extent of polytherapy with antiepileptic drugs in enrolled patients
- To study the medication adherence behavior among enrolled patients.

Review of Literature

Drug Utilization Review (DUR) / Drug Use Evaluation (DUE)

Drug Utilization Evaluation (DUE) has been defined by the American Society of Health System Pharmacists (ASHP) as a "criteria based, ongoing, planning and systemic process for monitoring and evaluating the prophylactic, therapeutic and empiric use of drugs to assure that they were provided appropriately, safely and effectively". DUE is a method by which information is retrieved to identify problems of drug use and also serves as a means to rectify the problem, there by contributing to rational drug therapy. DUE examines the process of drug administration, dispensing, outcomes of treatment, thereby helping the health care system to realize, interpret and ameliorate the prescribing, administration and utilization of medication".[24]

Drug utilization research is an essential part of pharmacoepidemiology as it describes the extent, nature and determinants of drug exposure. Hence, in recent years, studies on drug utilization have become a potential tool to be used in the evaluation of health care systems. The interest in drug utilization studies began in the early 1960s and its importance has increased since then because of increase in marketing of new drugs, wide variation in the pattern of drug prescribing and consumption, growing concern about delayed adverse effects and the increasing concern regarding the cost of drugs.[25]

DUR is an ongoing, systematic process designed to maintain the appropriate and effective use of medications. It involves a comprehensive review of a patient's medication and health history before, during, and after dispensing in order to attempt to achieve appropriate therapeutic decision-making and positive patient outcomes. Pharmacists participating in DUR programs can directly improve the quality of care for patients, individually and as populations, by striving to prevent the use of unnecessary or inappropriate drug therapy, prevent adverse drug reactions and

improve overall drug effectiveness. Other terms considered synonymous with DUR include Drug Use Evaluation (DUE), Medication Use Evaluation (MUE), and Medication Use Management. American Society of Health System Pharmacists (ASHP) currently espouses the nomenclature, Medication Use Evaluation (MUE).[26]

DUR is an authorized and structured ongoing review of practitioner prescribing, pharmacist dispensing and patient use of medications. The purpose of DUR is to ensure drugs are used appropriately, safely and effectively to improve patient health status. Predetermined criteria for appropriate drug therapy are compared against a patient‘s or a population‘s records. Non-adherence to criteria results in drug therapy changes. In addition, continual improvement in the appropriate, safe and effective use of drugs has the potential to lower the overall cost of healthcare. DUR allows the pharmacist to document and evaluate the benefit of pharmacy intervention in improving therapeutic and economic outcomes while demonstrating the overall value of the pharmacist.[26]

Drug utilization studies conducted in the inpatient settings are effective tools that help in evaluating the drug prescribing trends, efficiency, and cost effectiveness of hospital formularies. There is always a variation in drug utilization among different countries and even among health institutions within a country and sometimes within the same institute at different point of time, probably because of changing disease trends over a period of time. Conducting periodic studies of pattern of drug use in various hospital settings or patient populations is therefore essential to critically analyse the current hospital drug policies and to make recommendations based on various guidelines to improve upon the current drug usage pattern in the future, if needed. This is more importantly required in resource poor countries like India so as to ensure that the scarce

resources are utilized in the best possible manner. Though there has been various drug utilization studies conducted on specific populations and in varied settings in India.[27]

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 non-medical 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.[26]

Sources of drug utilization data:

Drug utilization data are available from databases since computerized or otherwise from these databases different types of information, qualitative or quantitative or referring to a particular population are available. Data may be diagnosis linked or non diagnosis linked. Diagnosis linked data gives information about drug consumption for a particular condition and outcome while non diagnosis linked data gives information only about drug consumption in a population. Some databases generate information about patterns of drug utilization and adverse drug reactions. Databases may also provide data in the form of drug sales, drug movement at various levels of the drug distribution chain, pharmaceutical and medical billing data or samples of prescription.

Such data are helpful in measuring the economic impact of drug use but does not provide information on the amount of drug exposure in the population. Data or information about sales are available through pharmacy records. They provide detailed information on the drugs but data on consumer is very limited. Also the data lacks information on morbidity. Data from general practitioners records of prescriptions can be more informative about the indications for drugs prescribed, diagnosis and other health related data, but these data are not always consistently completed. Data on drug utilization may also be obtained directly from the population through Health Surveys at National level or smaller surveys such as surveys conducted in specific settings such as among university students, female population, or elderly outpatients. Such studies provide information on drug use from consumer themselves and are a source of data on many other health related issues. Data obtained from medical practices and health facilities are used to measure specific aspects of health provision and drug use. Such data may be used to generate indicators that provide information on prescribing habits and aspects of patient care. These indicators may be used to determine where drug use problem exists, provide a mechanism for monitoring and supervision and motivate health care providers to follow established health care standards. Prescription and dispensing data are useful for determining some of the quality indicators of drug use recommended by WHO. These include-

- Average number of drugs per prescription (encounter).
- Percentage of drugs prescribed by generic name.
- Percentage of encounters with an antibiotic prescribed.
- Percentage of encounters with an injection prescribed.
- Percentage of drugs prescribed from essential drug list or formulary.
- Average drug cost per encounter.

Role of Pharmacist and other Health Care Practitioners in DUE Studies

Prospective DUR: This process places responsibility on the health care practitioner to conduct a review of the drug order when it is presented for filling and proactively resolve potential drug-patient problems. It affords the pharmacist or other health care practitioner the opportunity to interact with patients and members of the health care team to work on a treatment plan for each patient. In the retail and institutional settings, a pharmacist can assess the prescription order at the time of dispensing and, using information from the patient's medical and/or pharmacy record, determine the appropriateness of the drug therapy prescribed. If the pharmacist identifies opportunities for improved patient care, he/she can contact the prescriber to discuss treatment alternatives.

Concurrent DUR: The pharmacist and other health care practitioners have the responsibility in the concurrent DUR process to assess the ongoing therapy of the patient and, when necessary, intervene to help modify the patient's treatment plan. When caring for those patients with multiple diseases, case managers may become actively involved in the management of the patient's condition. Through interaction with the prescriber, a health care practitioner within a managed care organization can better understand the care plan the prescriber would like to follow. Through patient counseling, health care practitioners can offer education on the proper use of medications and determine if there are specific patient needs.

Pharmacists play a key role in this process because of their expertise in the area of medication therapy management. DUR affords the managed care pharmacist the opportunity to identify trends in prescribing within groups of patients whether by disease-state such as those with asthma, diabetes or high blood pressure, or by drug-specific criteria. Pharmacists can then, in

collaboration with prescribers and other members of the health care team, initiate action to improve drug therapy for patients.[28]

Definition of 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.[29]

Epidemiology

Next to stroke and dementia, epilepsy is the most common neurological condition seen by Neurologists all over the world, with higher prevalence in developing countries.[30] Worldwide, prevalence of the active epilepsy ranges from 4 to 5 per 1000 population and in India. The prevalence rate of epilepsy ranges between 4.15 and 7.03 per 1000 population. In newly diagnosed cases, 60% are partial and 40% generalized seizures. The incidence of epilepsy is quite high in pediatric population but the same decreases as children age. Over 10 million children worldwide are believed to have epilepsy. 30% of the children with seizures will have their first episode before the age of 4 years and more than half of the children with epilepsy will have more than one type of seizure.[31]

For children with epilepsy, seizures are often only one of the concerns. One in 4 children with epilepsy has some degree of intellectual disability.[32] In U.S each year, 200,000 new cases of epilepsy are diagnosed in that epilepsy affected 45,000 in children, younger than 15 years of age. The incidence is highest in those younger than age two and those older than age 65. Males are slightly more at risk than females.[33]

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 the ophylline, alcohol, high dose phenothiazines, antidepressants (especially maprotiline or buproprion), 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 duramater has been breached and in whom there is evidence of loss of conciousness), CNS infections, and stroke. Immunizations have not been associated with an increased risk of epilepsy.[34]

Classifications

I. Partial seizures (seizures begin locally)

A. Simple (without impairment of consciousness)

1. with motor symptoms

2. with special sensory or somato 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.[34]

Pathophysiology

Seizures result from excessive excitation, or from disordered inhibition of apopulation of neurons. Initially, a small number of neurons fire abnormally. Then normal membrane conductances and inhibitory synapticcurrents break down, excitability spreads locally (focal seizure) or morewidely (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-aminobutyricacid [GABA]), acetylcholine, norepinephrine, and serotonin)

Large numbers of generalized tonic-clonic (GTC) seizures (more than100) and multiple episodes of status epilepticus may be associated with neuronal damage. In particular, continued exposure to glutamate may contribute to neuronal damage.[35]

TREATMENT

General approach

- The treatment of choice depends on the type of epilepsy and on drug-specific adverse effects and patient preferences.

- Begin with monotherapy; about 50% to 70% of patients can be maintained on one antiepileptic drug (AED), but all are not seizure free.
- Up to 60% of patients with epilepsy are noncompliant, and this is the most common reason for treatment failure.
- Drug therapy may not be indicated in patients who have had only one seizure or those whose seizures have minimal impact on their lives. Patients who have had two or more seizures should generally be started on AEDs.
- Factors favoring successful withdrawal of AEDs include a seizure-free period of 2 to 4 years, complete seizure control within 1 year of onset, an onset of seizures after age 2 years and before age 35 years, and a normal EEG. Poor prognostic factors include a history of a high frequency of seizures, repeated episodes of status epilepticus, a combination of seizure types, and development of abnormal mental functioning. A 2-year, seizure- free period is suggested for absence and rolandic epilepsy, while a 4- year, seizure-free period is suggested for simple partial, CP, and absence associated with tonic-clonic seizures. According to the American Academy of Neurology guidelines, discontinuation of AEDs may be considered if the patient is seizure free for 2 to 5 years, if there is a single type of partial seizure or primary GTC seizures, if the neurologic examination and IQ are normal, and if the EEG normalized with treatment. AED withdrawal should always be done gradually. [35]

ANTISEIZURE DRUGS

Therapeutic aspects: The ideal antiseizure drug would suppress all seizures without causing any unwanted effects. Drugs used currently not only fail to control seizure activity in some patients, but frequently cause unwanted effects that range in severity from minimal impairment of the central nervous system (CNS) to death from aplastic anemia or hepatic failure. The task is to select the drug or combination of drugs that best controls seizures in an individual patient at an acceptable level of untoward effects. Complete control of seizures can be achieved in up to 50% of patients, while another 25% can be improved significantly. Success varies as a function of seizure type, cause, and other factors. To minimize toxicity, treatment with a single drug is preferred. Is seizures are not controlled with the initial agent at adequate plasma concentrations; substitution of a second drug is preferred to concurrent administration of a second agent. However, multiple-drug therapy may be needed, especially when two or more types of seizure occur in the same patient.[36]

Choice of antiepileptic in children: The use of antiepileptics in general in children has been reviewed. Again, appropriate treatment depends on seizure type, but there is a lack of evidence to support many therapeutic choices, in part because of the difficulties in undertaking studies in this population. In addition, children may be particularly susceptible to some adverse effects, including effects on behaviour, cognition, and development; behavioral problems have been associated particularly with Phenobarbital. None the less the principles of pharmacological management are similar to those in adults (above) although UK guidelines recommend that treatment should only be begun by a specialist.16 Dietary modification (the ketogenic diet) may also be tried.[37]

First-line treatment: Usually begins outside the hospital. It has been shown that pre hospital treatment of children reduces seizure length but often is not utilized. Benzodiazepines are the first-line drugs of choice in the treatment of CSE. If used within the first 20 min of seizure onset, termination rates of seizures can be as high as 70% to 85%. Because IV administration results in more rapid onset of action and improved bioavailability and efficacy, IV access should be obtained as soon as possible.

In hospital: IV lorazepam is usually the first-line treatment. It has a longer-lasting anticonvulsant activity and causes less respiratory depression than diazepam [17]. It has been shown to be more effective than diazepam or phenytoin in stopping seizures [18]. Note that repeat doses are much less likely to be effective (17% versus 85% for the first dose. If children have received benzodiazepines in the pre hospital setting, one repeat IV dose may be adequate before moving to second line treatments if necessary. Because timing is critically important,

Second-line treatment

Fosphenytoin/phenytoin is generally preferred over Phenobarbital because it is less likely to cause respiratory depression and alter the level of consciousness of the child, which can complicate the assessment. If no IV access is available, then IM for phenytoin, IO phenytoin or rectal paraldehyde are alternative options. Note that evidence for the safety and efficacy of IO phenytoin or phenobarbital is scant.[30]

Generalized Tonic-Clonic (GTC) Seizures

First-line treatment: Sodium valproate as first-line treatment. Offer lamotrigine if sodium valproat is unsuitable. If the person has myoclonic seizures or is suspected of having juvenile myoclonic epilepsy (JME), be aware that lamotrigine may exacerbate myoclonic seizures.

Consider carbamazepine and oxcarbazepine but be aware of the risk of exacerbating myoclonic or absence seizures.

Adjunctive treatment: Offer clobazam, lamotrigine, levetiracetam, sodium valproate or topiramate if first-line treatments are ineffective or not tolerated.

Absence Seizures

First-line treatment: Offer ethosuximide or sodium valproate as first-line treatment to children, young people and adults with absence seizures. If there is a high risk of GTC seizures, offer sodium valproate first, unless it is unsuitable. Offer lamotrigine if ethosuximide and sodium valproate are unsuitable, ineffective or not tolerated.

Adjunctive treatment: If two first-line AEDs are ineffective, consider a combination of two of these three AEDs as adjunctive treatment: ethosuximide, lamotrigine or sodium valproate.

Myoclonic Seizures

First-line treatment: Offer sodium valproate as first-line treatment, unless it is unsuitable. Consider levetiracetam or topiramate if sodium valproate is unsuitable or not tolerated. Topiramate has a less favourable side-effect profile than levetiracetam and sodium valproate. Adjunctive treatment: offer levetiracetam, sodium valproate or topiramate if first-line treatments are ineffective or not tolerated. If adjunctive treatment is ineffective or not tolerated, discuss with, or refer to, a tertiary epilepsy specialist and consider clobazam, clonazepam, piracetam or zonisamide. Do not offer carbamazepine, gabapentin, oxcarbazepine, phenytoin, pregabalin, tiagabine or vigabatrin.[38]

Treatment of women with epilepsy

Treatment of epilepsy in female patients needs special consideration as female hormones (i.e. estrogen and progesterone) by affecting neuronal excitability may alter seizure frequency. Cataminal epilepsy is a special problem in women. AEDs produce special problems in them (i.e. alteration in reproductive hormones producing anovulatory cycle, infertility and polycystic ovarian syndrome,aggravation of osteoporosis in elderly females by adverselyAffecting bone metabolism, potential teratogenicity, effect on the newborn as they cross into breast milk). In addition, pregnancy presents its own problem of unpredictable changes in seizure frequency, seizure recurrence related complications on pregnancy and altered drug pharmaco kinetics.

Treatment of epilepsy in Geriatrics

The elderly population, age more than 65 years, is the most rapidly growing segment of population. The incidence of epilepsy in them is approximately twice that in the younger population. They present special problems of altered pharmacokinetics, presence of co-morbid conditions requiring multiple medications (i.e. more chances of drug interaction) and misinterpretation of the interaction) and misinterpretation of the symptoms of drug toxicity as symptoms of co-morbid condition (i.e. Alzheimer's disease, stroke or metabolic encephalopathy). Hence proper selection of AEDs with optimal drug characteristics (i.e. no drug metabolism, a high therapeutic index and lack of drug interaction) is needed in elderly epileptics.

- Phenobarbitone and Primidone should not be used in elderly patients because of their sedative affects and adverse effect of cognition and mood to which this population is more sensitive. Of newer AEDs felbamate (hepatic toxicity and aplastic anemia) and vigabatrin (optic neuritis) should be avoided due to the side effects.

- Appropriate drugs for use in elderly epileptics are carbamazepine (withdose adjustment due to altered protein binding and altered hepatic metabolism), gabapentin (no drug interaction but dose is adjusted to renal functions), levetiracetam (no metabolism in liver, less protein bound i.e< 10%, lack of drug interaction, but dose to be adjusted to renal function), and lamotrigine (no dose adjustment required as hepatic glucuronide conjugation is only slightly diminished with age). Due to altered pharmacokinetics (i.e. altered protein binding & hepatic metabolism) the dose of Phenytoin, Carbamazepine, and valproate should be reduced. The frequency of administration should also be reduced when using drugs with short half-life, e.g. carbamazepine. Dose of AEDs having renal route of elimination ((e.g. Gabapentin, Levetiracetam) and both hepatic and renal elimination (e.g. Topiramate, Zonisamide) should be adjusted accordingly.

Status Epilepticus: Status epilepticus refers to continuous seizures or repetitive, discrete seizures with impaired consciousness in the interictal period. The duration of seizure activity sufficient to meet the definition of status epilepticus has traditionally been specified as 15 to 30 min. Status epilepticus is an emergency and must be treated immediately, since cardio respiratory dysfunction, hyperthermia, and metabolic derangements can develop as a consequence of prolonged seizures, and these can lead to irreversible neuronal injury. Furthermore, CNS injurycan occur even when the patient is paralyzed with neuromuscular blockade but continues to have electrographic seizures.

Initial management, it is important to secure the airway and give oxygen as required, assess cardiac and respiratory function, and establish intravenous access. Blood glucose should be assessed and any hypoglycemia corrected with glucose; intravenous thiamine should be given if there is any suggestion of alcoholabuse or inadequate nutrition. Initial antiepileptic treatment is

usually with a benzodiazepine. Although diazepam has been widely used in the past, intravenous lorazepam is now preferred for first-line treatment in most protocols, as it appearsto be more effective and has a longer duration of antiepilepticaction. Rectal diazepam or buccal midazolammay be used in the home setting or where intravenous access is not available (Rectal diazepammay also have a role in this setting to treat acute repetitive eizures, which may evolve into status epilepticus).Both midazolam and lorazepam have also been given intranasally For sustained control in patients with established epilepsy their usual antiepileptic regimen may be given orally or by nasogastric tube once immediate control is established, mor if necessary, for those drugs with an intravenous formulation, parenterally. In other patients, or in patients with established status not abolished by the benzodiazepine, additional treatment with one of several first-line anti epileptics is normally required. The choice is usually between intravenous phenytoin, fosphenytoin, or phenobarbital, allof which are effective. Repeat doses may need to be given. Although there is some evidence that Phenobarbital is more effective than phenytoin in abolishing seizures, many favour the use of the barbiturate only in patients who do not respond to phenytoin or fosphenytoin, because of the risk of severe respiratory depression. ECG monitoring is required in patients given intravenous phenytoin or fosphenytoin.

Febrile Convulsions: Febrile convulsions have been defined as epileptic seizures occurring between the ages of 6 months to 5 years and associated with a fever arising from an infectious illness outside the CNS. They usually occur during the rising phase of fever early in the course of the infection and are not considered to be a form of epilepsy. Febrile convulsions are considered to be benign if limited to a single tonic or tonic-clonic seizure lasting less than 15 minutes without any focal characteristics. About one third of children who have a benign febrile convulsion will have a recurrence. Risk factors for recurrence include an young onset age, a

history of epilepsy or febrile seizures in a first-degree relative, subsequent episodes of fever, and a first complex febrile seizure. The risk of developing epilepsy is low, but nevertheless it is 2 to 3 times greater than the risk in the population as a whole. Unless they are recurrent, benign febrile convulsions need only simple treatment to lower body temperature, such as that described under Fever and Hyperthermia. The prophylactic use of antiepileptics in children thought to be at risk of recurrence of febrile convulsions remains controversial. Many consider that even if recurrences can be prevented there is no evidence that the risk of developing epilepsy is reduced. A working group of the Royal College of Physicians and the British Paediatric Association considered that pooled analyses of studies of the prophylactic use of phenobarbital or sodium valproate showed that long-term prophylaxis was rarely indicated. Although some have found that intermittent prophylaxis with phenobarbital or diazepam given at the onset of and during fever could prevent recurrence of febrile convulsions, the working group did not recommend their routine use in this way. Other workers have found that giving paracetamol as an antipyretic and diazepam for intermittent prophylaxis failed to prevent recurrences of febrile convulsions. A later meta-analysis concluded that neither continuous nor intermittent prophylaxis could be recommended as the benefits did not outweigh the potential adverse effects, a view endorsed by the American Academy of Pediatrics. [36]

Juny Sebastian et al., conducted a study to assess the antiepileptic drugs (AEDS) usage, drug related problems and medication adherence behavior in epileptic patients. The data of 439 patients was reviewed, Morisky's Medication adherence scale was applied to study the medication adherence behavior of enrolled patients and those patients were also monitored to identify the adverse drugs reactions. Monotherapy was initiated in 61.9% patients, and when proven ineffective in controlling seizures dual therapy was initiated in 28.7% of patients and three drug therapy in 8.4% patients. Forty five adverse drugs reactions were reported during the study period. Phenytoin (53.3%) and valproic acid (26.7%) were the major drugs implicated for adverse drugs reactions. During the follow up visits, 96.6% of the patients were highly adherent to the prescribed medications, although less than half of the patients attended outpatient follow up.404 (92.2%) were inpatients and 35 (7.9%) out patients. A total of 646 AEDS were prescribed during the study period, In this study population, 74 (62.4%) patients received monotherapy, 126 (28.7%) patients received dual therapy, 38(8.7%) patients receive three drug therapy and only one patients was prescribed four drugs for the management of epilepsy.[30]

Akinsulore A et al., reviewed that epilepsy is a chronic disorder characterized by intermittent and also unpredictable seizures that are embarrassing and disruptive to the routine activities. This review was undertaken to provide information regarding prevalence, seizure types, treatment issues and psychosocial impact of epilepsy in Nigeria. We searched the PUBMED database
With emphasis on studies conducted in Nigeria, 48 relevant studies that met the criteria were reviewed. The point prevalence of epilepsy varies from 5.3 to 37per 1000 in Nigeria. Most studies showed a predominance of generalized tonic-clonic seizures. Nigerian patients with epilepsy suffer social deprivation and discrimination in education, employment, housing, marital

life as well as associated psychiatric morbidity. The review included the 48 relevant studies that met the criteria. Most studies showed a predominance of generalized tonic-clonic seizures. It was concluded that epilepsy, a stigmatizing disorder in Nigeria has a significant impact on the day to day functioning of those with the disorder.[39]

Sidig A et al., studied on people with epilepsy those are suffering from a unexplained negative impacts on their lives; due to misunderstanding of the disease and from the associated stigma. The study had the objective to assess the knowledge, attitude and practice among relatives of Sudanese epileptic patients. This descriptive cross-sectional community based study included 313 respondents. One third mentioned a brain lesion as the underlying cause of epilepsy. Most of the respondents mentioned loss of consciousness as the major symptom. More than two thirds mentioned that it is not contagious. Most of the respondents claimed that it can be controlled, and two thirds preferred medical treatment. The study revealed that half of the respondents had shown favorable attitudes and practice. The study revealed that the level of knowledge, attitude, and practice towards epilepsy needs community educational programmes to fill the gaps, and minimize the stigma .One third of respondents mentioned a brain lesion as the underlying cause of epilepsy and they also mentioned loss of consciousness as major symptom.[40]

Lakshmi C et al., studied on the physician prescribing pattern in pediatric seizures with the objective to educate the patient care taker about the disease and the use of drugs in order to control seizures and improve the quality of life. A non invasive prospective observational study included 86 pediatric patients Females were found to be more prone to seizures; prevalence of seizure was more in children aged 1-5 years old. Febrile seizures (46.5%) are the most

commonly observed type of seizure in children followed by tonic – clonic seizures (21%) and complex partial seizures (14%). The other types of seizures observed are simple partial seizures (7%), status epilepticus (2.3%) and others (9.3%). Febrile seizures are common types of seizure in children followed by tonic-clonic seizures and complex partial seizures.[41]

Elberry A Ahmed et al., evaluated the efficacy and tolerability of Levetiracetam (LEV) as an adjunctive therapy in pediatric patients with different generalized epilepsies. The study consisted 22 consecutive children age 4-19 years treated with LEV for at least 1 year. Of the 22 patient reviewed, 13 (59%) were boys and 9 (41%) were girls. Predominant seizure types were generalized tonic–clonic seizures 13 (59%) and tonic seizure 6 (27%). Other seizure types included myoclonic seizures 2 (9%) and focal seizure 3 (5%). The results showed 10 (45%) had become free of seizure for almost 7 months to 1 year. Eight of these 10 patients (80%) had normalized EEG. Seizure frequency was reduced in 9 (41%) patients and 3 (14%) patients still had seizure. No side effects were reported related to LEV treated patients except for 1 patient. The results showed seizure frequency reduction in 9 patients and 3 patients still had seizure and no side effects were seen with LEV except for 1 patient.[42]

Jeffery W Briton and Jerry J Shih., reviwed anti epileptic drugs and suicidality and found that risk of suicidal tendency in patients with epilepsy was significantly higher than the general population. In 2008, the U.S. Food and Drug Administration (FDA) published a warning after a meta-analysis of data from all clinical trials involving AEDs found a suicidality risk of 0.43 per 1000 patients in active drug arms of these clinical trials compared to a rate in the placebo arm of 0.22. While an increased risk for individual AEDs was found in two, the FDA decided to issue a

warning for the entire AED class. In this study, based on a cohort of 44,300 epilepsy patients, 453 cases with suicidal behavior or self-harm were matched with 8,962 controls.While this decision and the meta-analysis findings have been considered controversial, and have created concern that this stated risk may dissuade use of AEDs by patients who would benefit from them, it has led to increased awareness of the risk of suicidality and psychiatric co-morbidity in this patient group.[43]

Daniel F Connor, Kaan R.et al., Conducted a study on the prevalence and patterns of use of psychiatric and anticonvulsant medications were studied in 83 seriously emotionally disturbed children and adolescents at the time of their admission to a residential treatment facility. Youths (aged 5–19, mean = 13.6 years), consecutively admitted over 17 months, were assessed for the prevalence and patterns of use of psychotropic and anticonvulsant treatments. At admission, 76% of the youths were receiving psychiatric pharmacotherapy, 40% with more than one psychiatric agent, and 15% with a combination of psychotropic and anticonvulsant medications. Frequently prescribed medications were neuroleptics (35% of the medicated youths), sedative-hypnotics (26%), and anticonvulsants (15%) consecutively admitted over 17 months, were assessed for the prevalence and patterns of use of psychotropic and anticonvulsant treatments. At admission, 76% of the youths were receiving psychiatric pharmacotherapy, 40% with more than one psychiatric agent, and 15% with a combination of psychotropic and anticonvulsant medications. Frequently prescribed medications were neuroleptics (35% of the medicated youths), sedative-hypnotics (26%), and antidepressants (22%) were under-prescribed relative to their diagnostic indications. Over 50 different medication combinations were used. The neuroleptic + lithium combination was most common (25% of the polypharmacological treatments). Neuroleptics were the most

commonly prescribed medication and mostly used for nonpsychotic, and nonbipolar indications (55% of neuroleptic trials). Neuroleptics were used primarily for aggression regardless of diagnosis. Neuroleptics were used more in symptomatic treatments than in treatments for indicated diagnoses.[44]

Murthy NV et al., investigated the anti epileptic drugs use in epilepsy with a particular attention towards exposure of AEDs, gender and age differences and changes in prescription patterns over time. The study included 150 patients along with the collection of patient IDs, number of prescriptions, date of prescriptions, type of prescriptions, reimbursement code, age groups and gender and medication history, and demographic details of the patients as for protocol. The demographic details of our study population, males 79 (52.6%) are more prone to epilepsy than the females 71(46.3%). Generalized –tonic-clonic seizure type is the most common type of epilepsy which contribute(49.3%), and for this type of epilepsy Sodium valproate was most commonly prescribed (14.6%), followed by simple partial seizure 24 (16%) and Carbamazepine (13.3%) was the first line drug prescribed for simple partial seizures and complex partial seizures although Phenytoin was used sporadically. Prescription patterns were consistent with current evidence about the spectrum of efficacy of individual AEDs in different epilepsy syndromes. The high prevalence of polytherapy, including combinations of three or more AEDs, is a cause for concern. The study found that Generalized-tonic-clonic seizure type is the most common type of epilepsy for which sodium valproate was prescribed, followed by simple partial seizure for which carbamazepine was prescribed as first line drug.[7]

Sanjeev V. Thamos et al., conducted research on frequent seizures and polytherapy and concluded that the drugs prescribed for GE were Valproate (VPA)36 (76.6%), Phenytoin (PHT) 6 (12.8%) ,Phenobarbitone (PB) 3 (6.45%), Corbamazepine(CBZ) 3 (6.4%) and Clonagepan (CZP 02 (4.3%), while those for LRE were CBZ 45 (69.23%) ,Clobazam (CLB) 15 (23,1%), PHT 14 (21.5%) ,PB10 (15.4%),VPA 4 (6.2%) and CZP 1(1.5%). Between primary drugs (CBZ, VPA, PHT AND PB) decreased while combination of primary drug (mostly CBZ) and CLB increased at the time of last fallow up when compared to entry to the referral centre.[45]

Rena PVS. Carried a study on medical management of epilepsy and concluded that treatment of epilepsy is a complex and challenging problem. Selection of AEDs should be appropriate to patient, seizure type and epileptic syndromes and noncompliance is responsible for failure in over one third of patients Application of pharmacokinetics principles while administering these drugs is an essential requirement. Monotherapy with appropriate AEDs for seizure types and epileptic syndrome is the initial treatment of choice. The ultimate goal of reversing preventing the manifestation of epilepsy (i.e. epilepsy cure) is still not an obtainable target with AEDs. There is resurgence of "rational polypharmacy" in the treatment of epilepsy .Other modes of therapy, including surgery, are still needed in those remaining refractory to medical treatment.[46]

K R Chalapathi et al., conducted a study on Clinical and radiological evaluation of new-onset epiletic seizures in a tertiary care hospital. This cross sectional study was studied in 100 adult patients, presenting with seizures attending the Emergency department, General Medicine and Neurology wards and OPD during the period of March 2006 to March 2008. 63% of patients were in the age group of 20-39 years, 63% were males and 37% were females. 65% presented

with GTCS, 35% with partial seizures. They concluded that Generalized Tonic clonic seizures were the commonest type of seizures was present, seen mostly in male patients. Initiating the treatment with antiepileptic drugs was left the sole discretion of the treating physician for a case of new onset seizures.[47]

T Badwaik R et al., Conducted a study on a drug utilization study of antiepileptic drugs use in a tertiary care hospital at NKPSIMS and RC, Nagpur India. The main objectives of the study were to describe the drug utilization pattern of anti-epileptic drugs. The present study was a prospective, non-randomized controlled single blinded trial, Out of 146 participants, 76 were male and 70 were females. Monotherapy was given in 102 patients (69.8%) while polytherapy was given in 44 patients (30.1%). Amongst the monotherapy, phenytoin was most commonly prescribed in 25 patients (17.1%) while levetiracetam and vigabatrin were least prescribed (1.3 and 2.7 respectively). Amongst the fixed dose combinations (FDCs) phenytoin plus phenobarbital was most commonly prescribed. They concluded that the findings of the present study should be generalized by performing such regular studies elsewhere in other parts of the country, so as to help in meticulous planning in order to reduce the expenditures in health care without affecting efficacy.[48]

M V Yogesh et al., conducted a study on drug utilization pattern of antiepileptic drugs and direct and indirect cost estimation in the treatment of epilepsy at tertiary care hospital at Maharashtra. Current study was done to observe prescription pattern and cost of epilepsy management to the patients. A prospective observational questionnaire based cross sectional survey was conducted in neurology OPD for 12months. A demographic profile and prescription

data of AEDs for past 1 year were collected from diagnosed cases of GTC, CPS and SPS for at least 1 year of treatment. WHO indicators were used for analyzing current prescriptions and direct and indirect cost of treatment for past 1 year was analyzed. A total of 275 AEDs were prescribed to 138 patients. GTC was most common condition with 43.47%. Average no. of AEDs prescribed per encounter was 1.99 with 52% of newer AEDs. Phenytoin was commonly prescribed (24%) for GTC and SPS with secondary generalization. Valproate was commonly prescribed for CPS while carbamazepine for SPS. Average consultation time was app. 15 minutes. 98% of patients had correct knowledge of drug dosage. An average total cost borne by patients was Rs. 14589 per year which constitutes to 53% of per capita income. It concluded that older antiepileptic drugs are still commonly prescribed drugs. High prescription of brand names and prescription of drugs outside of hospital formulary as only limited drugs are available on schedule list, may be the reason for cost burden to epileptic patients.[4]

Mazhar F et al., conducted a study on drug utilization evaluation of antiepileptics in three selected multidisciplinary teaching hospitals of Pakistan. Aim of the study was to identify the utilization pattern of antiepileptic drugs (AEDs) in a representative sample of the Pakistani population. To highlight the main risk factors associated with different forms of epilepsy , retrospective drug utilization review study was conducted at three teaching institutions of Karachi. During the nine months study period, epileptic and non-epileptic patients who were prescribed with AEDs were enrolled consecutively. Data were collected through the integration of computerized records and standard proforma to retrieve information on age, gender, diagnosis, type of seizure and AEDs data. The results were analyzed by univariate statistics. Total 622 patients i.e., 426 epileptic and 196 non-epileptic patients who were prescribed with AED were

analyzed in the study. The age ranged from 0.1 to 82 years (median, 36), there were 56% male and 44% female patients. Simple partial seizure (28%) was most common type of seizures. Monotherapy accounted for 77% of total epileptic patient. Idiopathic/cryptogenic was most common etiology of epileptic seizure (41%). CNS infections (57%) were leading cause of symptomatic epilepsy. Most prevalent utilization for non-epileptic condition was neuropathic pain (55%). In epileptic patients, Valproate (17%) and Diazepam (14%) whereas in non-epileptic patients, Gabapentin (26%) and Pregabalin (20%) was most commonly prescribed drugs. It concluded that despite the availability of newer antiepileptics in Pakistan, the domain of classic agents was still dominated in pharmacotherapy of epileptic seizure. The utilization patterns reported here are in agreement with general guidelines except for extensive prescribing of diazepam and some drug that use off label.[8]

N Friedman J et al., conducted a study on Emergency management of the paediatric patient with generalized convulsive status epilepticus. They concluded that there have been a number of changes in the emergency management of CSE (Convulsive Status Epilepticus) over the past 15 years based on the emergence of new evidence and medications. It is important for all those involved in the acute medical management of children to have an up-to-date, evidence-based approach to the emergency management of children with CSE.[32]

Arulkumaran SG et al., conducted study on a drug use evaluation of anti-epileptics at a multispecialty tertiary care teaching hospital at Coimbatore. A prospective observational study was conducted at a multi-disciplinary, super-specialty corporate hospital. The total study population was 268, for a period of 8 months from July 2008 to February 2009 in the group of

patients suffering from generalized tonic-clonicseizures, Sodium valproate was the most frequently prescribed AED (Anti-Epileptic Drug). The demographic data revealed that number of male and female patients were 63% (170) and 37% (98) respectively. The age ranged from 02 - 82 yrs with 48% (129) of patients being middle aged between 31 and 60. 6% (16) of patients were newly diagnosed cases of epileptic seizures. Monotherapy was most frequentlyused in all types of epileptic seizures. The selection of the AEDs corresponds well with the known efficacy profile for specific epileptic seizure types. The most commonly prescribed AED as Sodium valproate, followed by Carbamazepine, Phenytoin for epilepsy. Most epileptics can be effectively managed with the conventional oral AEDs.[49]

Jena M et al., conducted study on Monitoring of Prescriptions and pharmacovigilance evaluation of antiepileptic drugs in a tertiary care teaching hospital. The aim of the study was know about epidemiological profile, prescribing patterns of AEDs and adverse drug reaction profile and outcome in both adult and pediatric patients. This was a cross-sectional clinico-epidemiological observational study of epilepsy patients over 1 year in neurology & pediatrics outpatient departments. The prescriptions from 820 patients containing AEDs were analyzed. Most of patients are in pediatric age group and were more common in male. Dual therapy (45.4%) was the most common regimen followed by polytherapy and monotherapy (26.5%). Valproic acid (43.1%) was the most frequently prescribed AED followed by Phenytoin (38.04%). Number of adverse drugs reactions reported was 122. Phenytoin and Valproic acid were the major drugs implicated for adverse drugs reactions. This study strongly concluded that highlights the need for therapeutic drug monitoring of epileptic patients. Measures should be taken to improve rational use of antiepileptic drugs to minimize the number of refractory cases of epilepsy.[23]

Viswanathan S., carried out study at Delhi to assess the prescribing pattern of AEDs in pediatric outpatient department and to record the seizure control and ADRs. This study included 200 patients and all were followed up for 3 months for seizure control and ADRs. Regarding treatment with AEDs 87.5% received monotherapy and 12.5% combination therapy. Among monotherapy, 63.5% were prescribed Valproate, 20.5% Carbamazepine, 2.5% Phenytoin. In combination therapy Valproate with Clobazam (8.5%) and Valproate with Levetiracetam (1%) were prescribed. In generalized epilepsy 89.5% and 50% of children showed good control with monotherapy and combination therapy respectively. For partial epilepsy 98.2% had good control with monotherapy and 66.7% with combination therapy. The results showed that monotherapy was more effective and safe as compared to combination therapy to treat generalized and partial epilepsy in pediatric population. Also it was found out that valproate was the most commonly prescribed drug for generalized seizures and Carbamazepine for partial epilepsy in both monotherapy and combination therapy.[50]

N Maity et al., conducted study at Bangalore to assess Trends in Utilization of Antiepileptic Drugs Among Pediatric Patients in a Tertiary Care Hospital. The study was a retrospective observational study carried out, among pediatric epilepsy patients There was a relative male preponderance (56%) seen among epileptic patients. Of the total 210 patients analyzed, 110 (52.4%) were having partial seizure and 100 (47.6%) had generalized seizures. Out of 210 patients 134 (63.8%) were on mono-therapy and 76 patients (36.2%) were on polytherapy. Mean daily doses of carbamazepine were 492.69±51.8 and 320.97±42.09 in polytherapy and monotherapy respectively. The serum levels were mo-nitored for commonly used antiepileptics like phenytoin, carbamazepine, phenobarbitone and Valproate in 43 (20.5%) patients. Among

210 patients, antiepileptic drugs were changed for 96 (45.71%) and the reasons for changing prescriptions were uncontrolled seizures (67.7%), recurrence (22.9%) and adverse effects (9.3%).A nationally based study and guidelines may bring a more rational approach for antiepileptic drug. it concluded that Though most epilepsy can be effectively managed with conventional antiepileptic, an increase in experience with the use of newer medications can offer an additional ad-vantage to patients.[51]

Purcell B et al., conducted a study on the prevalence of treated epilepsy and in use of new antiepileptic drugs (AEDs) in England and Wales between 1994 and 1998 using the General Practice Research Database**.** The age-standardized prevalence of epilepsy in 1998 was 7.4 per 1,000 in males and 7.2 per 1,000in females, and increased by 7per cent between 1994 and 1998. The percentage of patients prescribed newer AEDs increased from 6.8 per cent to11.9 per cent in males and from7.5 per cent to 13.7 per cent in females over the same period. In1998, the use of newer AEDs was highest in those aged 5 to 15 years and lowest in the elderly. The prevalence of epilepsy was highest in deprived areas. The estimated number of patients with epilepsy in England and Wales in 1998 was 400,000 of which 50,000 (13 per cent) received new AEDs in 1998.An increased percentage of patients were prescribed newer anti-epileptic drugs between 1994 and 1998, but this was restricted to younger age groups. Age-specific side effects, such as liver toxicity from sodium valproate in children, may mean newer AEDs are tried as first line agents. It will be important to monitor these trends as new drugs continue to be made available.[3]

Getachive H et al: conducted a study on Medication adherence in epilepsy and potential risk factors associated with non adherence in tertiary care teaching hospital in southwest Ethiopia. In this study main objective is to determine adherence rate to antiepileptic medications and identify the potential risk factors associated with non-adherence in Jimma University Specialized Hospital/JUSH. This was hospital based cross-sectional study conducted on 265 patients using patients self report and pharmacy refill record. The self report involved the structured patient interview after verbal informed consent was obtained. Data were Analyzed using SPSS for windows version 16.0. Chi-square test was used to observe the association of variables with adherence. The adherence rate of patients (n=265) to association of variables with adherence. The adherence rate of patients (n=265) to antiepileptic drugs/AED was found to be 63.2% based on their refill records, compliant fill rate. On the basis of patient's self report for their pattern of drug use, 155 (58.5%) patients reported that they had never missed (neither daily dose nor time of taking), 78 (29.4%) missed daily dose some times, 12 (4.5%) missed only time of taking, and 7.5% (n=20) missed both time of taking and daily dose sometimes. The most common reasons for missing dose were forgetfulness (31.8%) followed by being busy (20.9%). Sedation (39.4%) was the commonest side effect faced by the patient. The rate of adherence absorbed in this study was low. Pill burden, co-morbid conditions and appointment missing were found to affect adherence.[52]

Rishel W et al: A study conducted on drug use evaluation of antiepileptic drugs in outpatient epilepsy clinic of Bishofu general hospital, East Shewa, Ethiopia. The purpose of this study was to evaluate use of antiepileptic drugs in epilepsy Outpatient Clinic of Bishoftu General Hospital (BGH), East Shewa, it was a retrospective cross-sectional study was applied and all the

necessary data was collected from the epileptic patient cards using the pre-developed data collection format. The data collection was conducted from March 10 to April 10, 2014. Results of this study include a total of 259 patients' information cards which contain AEDs were studied. Among them 135 were males and 124 were females. Out of total 15, 65, 172and 7 of the patients were in the age group of < 5, 5-18, 19-65 and > 65years, respectively. Generalized tonic-clonic (48.6%) were the most common type of epileptic seizure seen. Monotherapy (88%) was most frequently used. Headache (47.8%) was the commonest adverse effect complained by the patients. The most commonly prescribed AED was Phenobarbitone (92.8%), followed by Phenytoin (3.8%). Fifty four percent (54.4%) of AED use was in accordance with the indicationset in the national standard treatment guideline while 2.9% were inappropriate. Also, 121(44%) of the indications were found to be difficult to know whether they are correct or incorrect indications since the type of epilepsy was not identified & written on the patient card. There were 16.5% under dose, 1.1% over dose and 12.7% AED use was with incorrect duration. There were potential drug-drug interactions in 5%. The present study has attempted to reveal the practical use of AEDs in epilepsy Outpatient Clinic of Bishoftu General Hospital (BGH), East Shewa, Ethiopia. Consequently, the classification of seizure as well as the use of drugs with potential drug interaction, dose and duration problem needs urgent interventions. Ethiopia.[53]

Shaik R et al: conducted a study of anti-epileptic therapy in pediatric patients in a secondary care hospital the present study was undertaken to get an overview of the current trends in prescribing patterns of anti-epileptic drugs (AEDs) in the treatment of epilepsy in pediatrics department, St. Martha's Hospital, Bangalore. A nine month prospective method of study was carried out in St. Martha's Hospital, Bangalore after obtaining Ethical Committee Clearance.

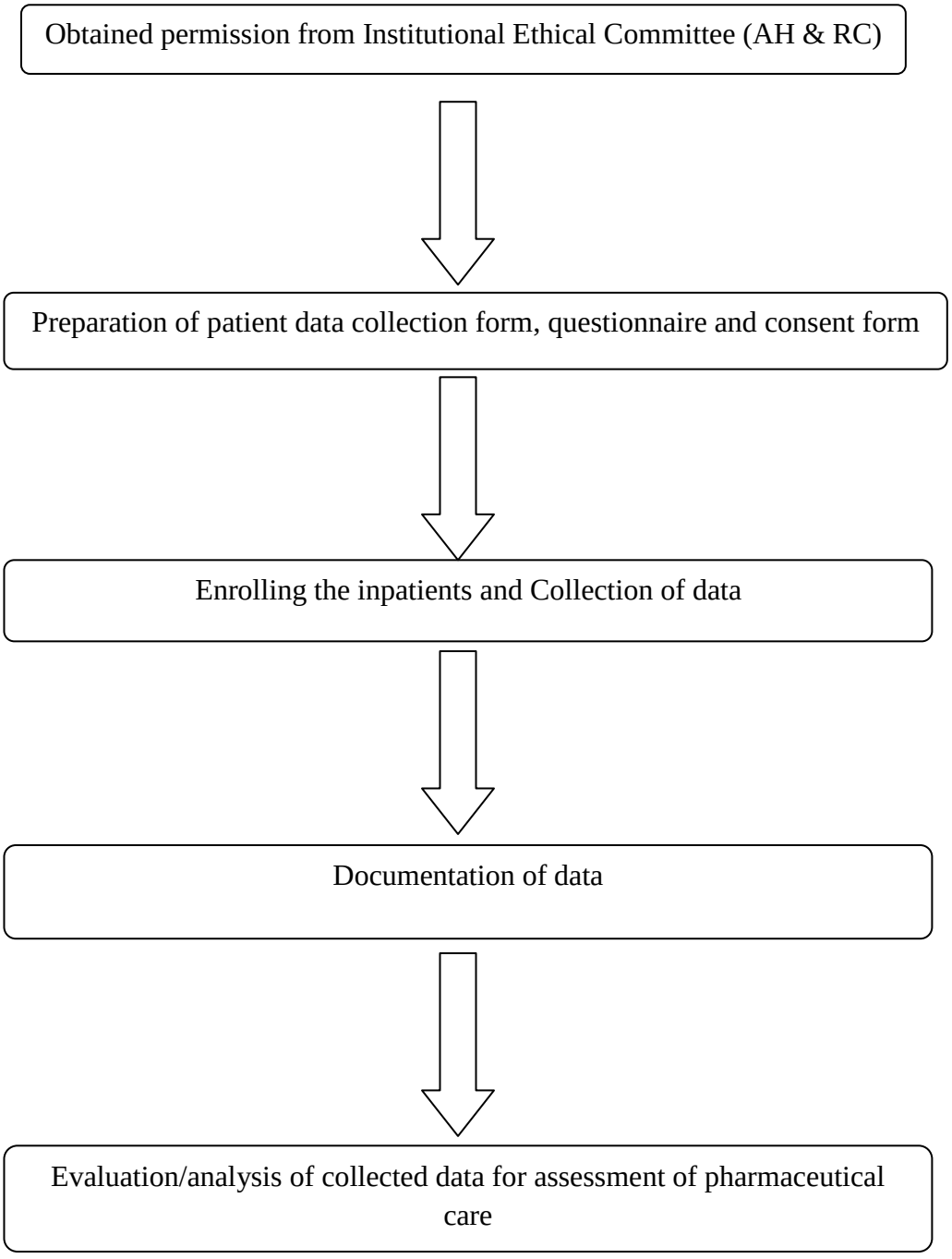
Patient's data was collected from the out-patient cards and in-patient case sheets who were prescribed with anti-epileptic drugs. Results of this study were Out of 110 patients during the study period, 66% were male and maximum number of patients 45(41%) were in the age group of 1-12 months. With respect to pharmacotherapy, 54 (49.1%) patients were subjected to acute management, 2 (1.8%) patients were given prophylactic treatment and the remaining 54(49.1%) patients were grouped under long-term therapy. Under acute management, Lorazepam (98.2%) was prescribed in maximum number of patients. Clobazam was given as prophylactic therapy in2(1.8%) patients. For the long-term management of seizures, monotherapy was seen in maximum number of patients (70.3%) followed by dual therapy (22.3%) and polytherapy (7.4%). Details of monotherapy revealed that phenobarbitone was prescribed for maxumim number of patients (50%) followed by phenytoin (39.5%) and valproate (5.3%). Newer anti-epileptic drugs like levetiracetam and topiramate were also prescribed as a part of combination therapy. During the study period, a total of 3(2.7%) adverse drug reactions (ADRs) were reported. All the 3 ADRs were due to the same drug i.e. Phenytoin. Among the different approaches of treatment, monotherapy was found to be the most preferred choice of treatment. Most of the patients (60%) attended the follow-up and majority of them (95.5%) were found to be seizure free after the follow-up session indicating patient compliance.[31]

Waleed M. Sweileh et al: conducted a study on self-reported medication adherence and treatment satisfaction in patients with epilepsy. Medication adherence and satisfaction in patients with epilepsy in Arab countries are lacking. The main objective of this study was to assess medication adhere.nce and its relationship with treatment satisfaction, number of antiepileptic drugs (AEDs) taken, and epilepsy control in a sample of Palestinian patients. This cross-sectional descriptive study was carried out at Al-Makhfya Governmental Outpatient Centre in Nablus,

Palestine, during the summer of 2010. A convenience sampling method was used to select patients over the study period. Medication adherence was measured using the eight-item Morisky Medication Adherence Scale (MMAS); treatment satisfaction was measured using the Treatment Satisfaction Questionnaire for Medication (TSQM 1.4 Results of this study werea convenience sample of 75 patients was studied. On the basis of the MMAS, 11 patients (14.7%) had alow rate, 37 (49.3%) had a medium rate, and 27 (36%) had a high rate of adherence. Adherence was positively and significantly correlated with age (P=0.02) and duration of illness (P=0.01). Mean satisfaction with respect to effectiveness, side effects, convenience, and global satisfaction were 73.6±20.7, 82.4±29.8, 69.5±15.5, and 68.4±18.3, respectively. There were significant differences in mean values in the effectiveness (Pb0.01) and convenience (Pb0.01) domains, but not the side effect (P=0.1) and global satisfaction (P=0.08) domains among patients with different levels of adherence. Patients on monotherapy had significantly higher satisfaction in the effectiveness domain (P=0.04) than patients on polytherapy. Similarly, patients with well-controlled epilepsy scored significantly higher in the Effectiveness (P=0.01) and Global Satisfaction (P=0.01) domains than those with poorly controlled epilepsy. Conclusion of this study was that adherence to and a satisfaction with AEDs was moderate and was not associated with seizure control or number of AEDs.[5s]

Materials & Methods

STUDY FLOW CHART



METHODOLOGY

STUDY SITE

The present study was conducted in medicine and pediatrics departments of Adichunchanagiri Hospital and Research Center, B.G.Nagara. It is a 1030-bedded, tertiary care, teaching, service oriented hospital having different specialties like medicine all units, pediatrics in three units. This hospital provides specialized health care services to all strata of people in and around B.G. Nagara.

STUDY DESIGN

The study was a prospective and observational study.

STUDY PERIOD

This study was conducted for a period of 9 months.

STUDY APPROVAL.

Ethical clearance was obtained from the Institutional Ethical Committee of AH and RC, B.G.Nagara.

STUDY CRITERIA

Inclusion Criteria:

- All in-patients both sex prescribed with anti-epileptic drug in Pediatric & General medicine departments
- In-patients who are willing to participate in the study.

Exclusion Criteria:

- Pregnant/lactating women.

SOURCE OF DATA

Patient data relevant to the study was obtained from the following sources

- Patient consent form (Annexure c)
- Patient data collection form (Annexure b)
- Patient case note/prescription
- Lab reports
- Morisky medication adherence scale questionnaire

STUDY PROCEDURE

In-patients who met the study criteria were enrolled to the study for assessing drug utilization pattern after obtaining their written consent from patient/patient care taker in medicine units & pediatric units. A suitably designed data collection form was used to record all the necessary data including patient demographic details, patient medication history, and reason for admission, medication details and lab investigations.

ADR and Drug Interactions

The enrolled patient's (inpatients) case sheet was reviewed every day during ward round participation. Serious/major drug-drug interactions and Adverse Drug Reactions (ADRs) were identified by using standard text books like Harrison's principles of internal medicine 16th edition, Martindale the complete drug reference thirty-sixth edition, and MICROMEDEX softwares available in the department. The identified drug related problems were discussed with the physicians for further management.

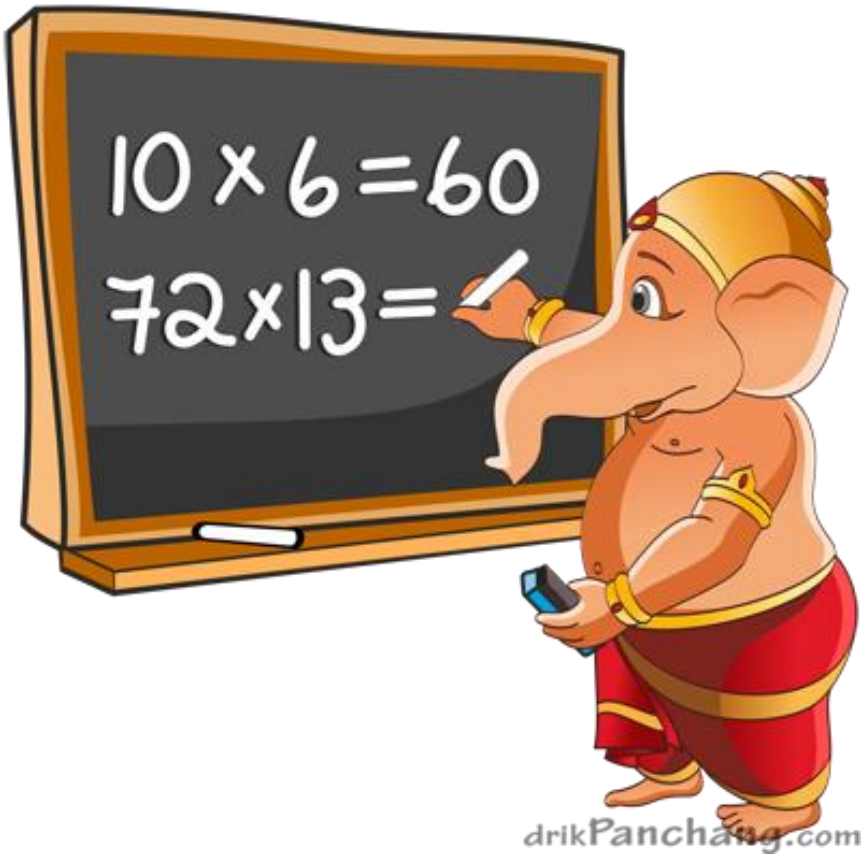
- Morisky medication adherence scale questionnaire: An 8 item adherence scale of Morisky DE was used and prior permission was taken before conducting the study.

- Morisky Medication Adherence Scale questionnaire. (Annexure e)

For every answer response of NO scored as 1 and for YES scored as 0 (questions 1, 2, 3, 4, 6, 7) and to reverse the code response in a positive direction for item 5 and standardize the code for item 8 (0-4), resulting in a scale from low adherence to high adherence. Item 8 is divided by 4 when calculating summated scores, like item 8=4 – 1, item 8=3 -0.75, item 8=2 – 0.50, item 8=1 – 0.25 and item 8=0 – 0 respectively.

STATISTICAL METHODS

The data were subjected to descriptive statistical analysis using Microsoft Excel. Microsoft word and Excel have been used to generate bar graph, pie charts and tables.



Results

A total of 120 patients admitted to pediatrics and medicine units prescribed with various antiepileptic drugs were reviewed over a period of 9 months from July 2015 -February 2016.

DEMOGRAPHIC DETAILS

Demographic details	**Frequency(N)**	**Percentage (%)**
Gender distribution		
Male	50	41.66%
Female	70	58.33%
Age distribution		
0 -18	70	58.33%
19 – 35	13	10.83%
36 - 60	22	18.33%
61 – 80	14	11.66%

Table No.1: Demographic details of patient: It showed that more pediatric patients (age group of 0-18) than adults and geriatric cases. (> 18 age group) were included in our study as shown in table. Females were more (58.33%) than male patients (41.66%).10.83% of people was within 19-35 age groups, 18.33% of people were within age group of 36-80 and 11.66% of people were within age group of 61-80. 58.33% of people were with age group of 0-18.

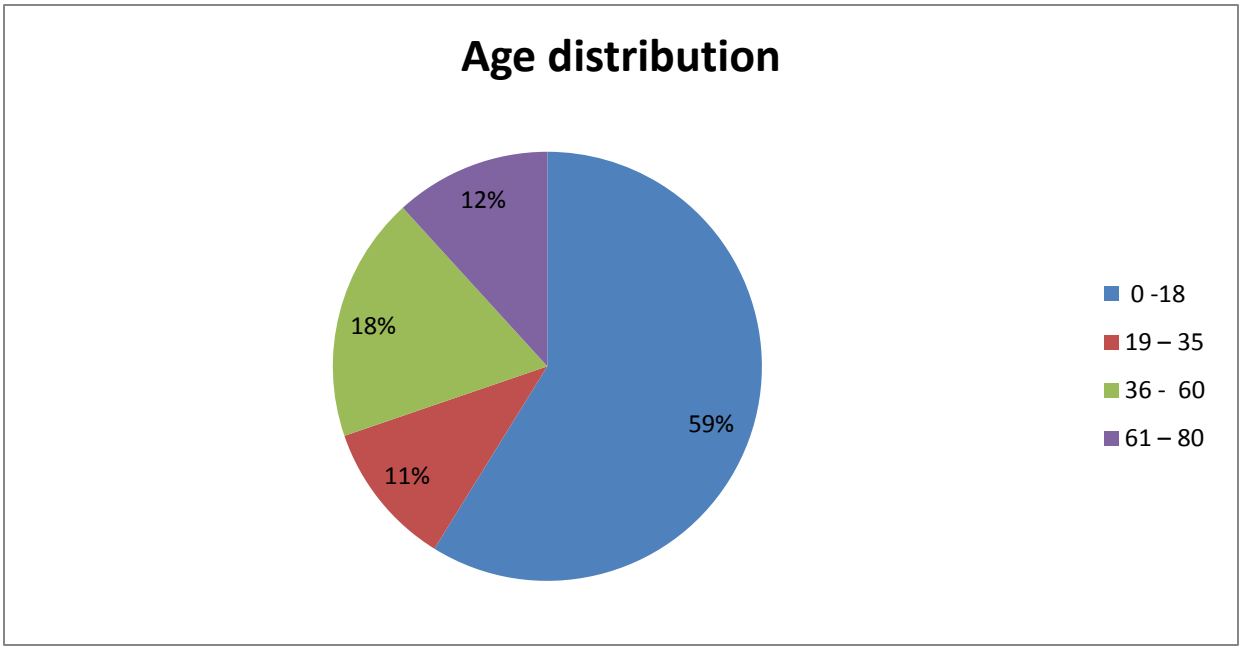


Figure No1: Age wise distribution of patients.

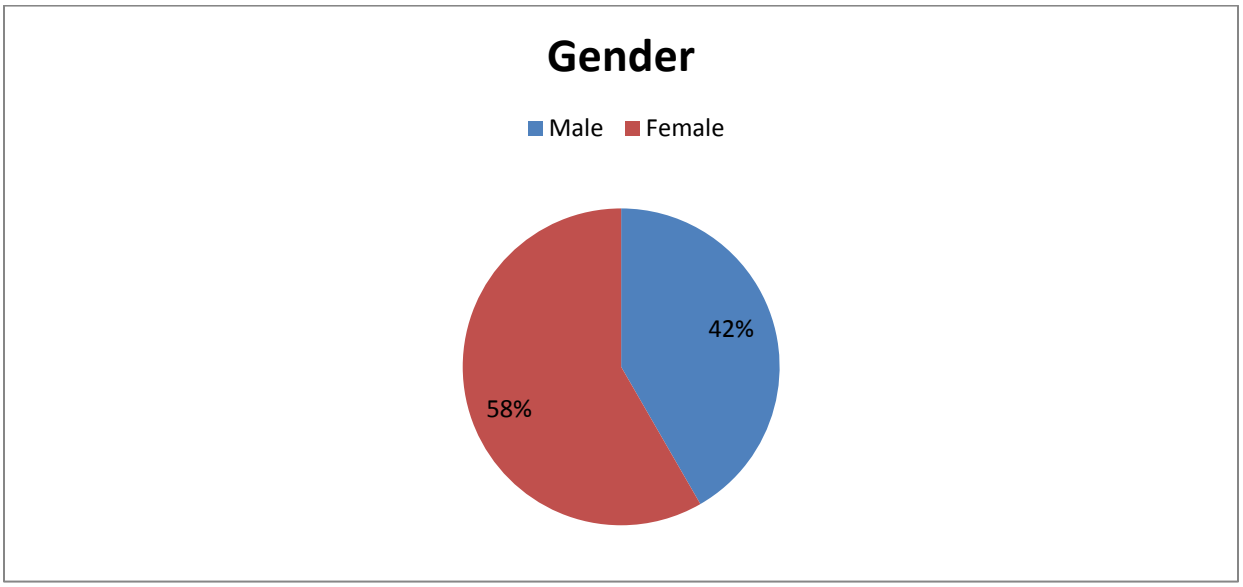


Figure No 2: Gender wise distribution of patients.

DISTRIBUTION OF DIAGNOSIS & CO-MORBIDITY CONDITIONS

Diagnosis	Frequency (N)	Pe yrcentage (%)
Epilepsy without co-morbidity	96	80%
Epilepsy with co-morbidity	24	20%
✓ Hypertension, Diabetes Mellitus	9	7.5%
✓ Cardiovascular accident,Hypertension,Diabetes melleitus	5	4.166%
✓ Meningitis	5	4.166%
✓ Alcohol withdrwal symptom	2	1.66%
✓ Viral fever and seizure	1	0.833%
✓ Migraine	1	0.83%
✓ Bronchopneumonia	1	0.83%

Table No.2: It showed that out of 120 patients 96(80%) were having epilepsy without any co-morbid condition and 20% were having co-morbidities like Hypertension(HTN) plus Diabetes mellitus (DM) (7.5%), Cardiovascular accident plus Hypertension plus Diabetes mellitus (4.1%), Meningitis (4.1%), Alcohol withdrawal symptom (1.66%) and Viral fever (0.83%), Migraine (0.83%), Bronchopneumonia(0.83%).

DISTRIBUTION OF EPILEPSY

Different forms of epilepsy	Frequency	Percentage (%)
Status epilepticus	9	7.5%
Partial Siezure	5	4.16%
Generalised tonic clonic siezures	44	36.6%
Generalised tonic clonic siezures by hot water	16	13.33%
Generalised tonic clonic siezures by alcohol dependence	3	2.5%
Fibrile seizures	16	13.3%
Atypical seizures	8	6.66%
Typical seizures	17	14.16%
Focal seizures	2	16.66%
Total	120	100%

Table No.3: It showed that generalized tonic clonic seizures (36.6%) followed by Atypical seizures (6.66%) Typical seizures (14.16%), Status epilepticus(7.5%), Partial Siezure (4.16%), hot water

epilepsy (13.33%) , alcohol dependence and Focal seizures (2.5%) were the different types of epilepsy encountered in our hospital.

INDICATION WISE UTILISATION PATTERN OF DRUGS AND POLYTHERAPY

Indication	Utilisation pattern of antiepileptics	Frequency(N) of patients	Status of polytherapy
Status Epilepticus	Phenytoin+Lorazepam	1	Polytherapy
	Phenytoin +Lorazepam+ Clobazam	1	Polytherapy
	Phenytoin + Phenobarbital	1	Polytherapy
	Phenytoin Only	2	Monotherapy
	Phenytoin +Valproate	1	Polytherapy
	Phenytoin +Levetiracetam+ Phenobarbital+ Midazolam	1	Polytherapy
	Phenytoin + Levetiracetam+ Midazolam	1	Polytherapy
	Phenytoin + Lorazepam + Phenobarbital	1	Polytherapy
			Monotherapy=2,Polytherapy=7
Partial Seizure	Phenytoin +Clobazam	1	Polytherapy
	Levetiracetam	1	Monotherapy
	Phenytoin +Valproate	1	Polytherapy
	Carbamazepine +Levetiracetam	2	Polytherapy
			Monotherapy=1,Polytherapy=3
Generalised Toinic Clonic Seizures	Phenytoin + Carbamazepine+ Lorazepam	1	Polytherapy
	Phenytoin +Carbamazepine	11	Polytherapy
	Phenytoin + Carbamazepine+Phenobarbital	1	Polytherapy
	Phenytoin	9	Monotherapy
	Phenytoin + Phenobarbital	3	Polytherapy
	Phenytoin + Clobazam	2	Polytherapy
	Phenytoin +Lorazepam	12	Polytherapy
	Phenyoin+Lorazepam + Clobazam +Levetiracetam	1	Polytherapy
	Phenytoin + Carbamazepine+ Clobazam	1	Polytherapy
	Phenytoin + Clobazam+ Valproate	2	Polytherapy

	Clobazam + Midazolam	1	Polytherapy
			Monotherapy=9,Polytherapy=35
Febrile Seizures	Carbamazepine + Lorazepam	2	Polytherapy
	Carbamazepine + Valproic Acid	1	Polytherapy
	Carbamazepine	6	Monotherapy
	Carbamazepine + Clobazam	2	Polytherapy
	Carbamazepine + Phenobarbital	1	Polytherapy
	Lorazepam	1	Monotherapy
	Lorazepam + Clobazam + Phenobarbital	1	Polytherapy
	Lorazepam + Phenobarbital	1	Polytherapy
	Lorazepam + Phenobarbital + Valproic Acid	1	Polytherapy
			Monotherapy=7,Polytherapy=9
Atypical Seizures	Lorazepam	1	Monotherapy
	Phenytoin`	1	Monotherapy
	Phenytoin +Lorazepam + Clobazam	1	Polytherapy
	Clobazam	4	Monotherapy
	Phenytoin +Carbamazepine	1	Polytherapy
			Monotherapy=6,Polytherapy=2
Typical Seizures	Lorazepam + Clobazam	3	Polytherapy
	Clobazam	7	Monotherapy
	Clobazam + Phenobarbital	1	Polytherapy
	Phenytoin + Lorazepam	1	Polytherapy
	Phenytoin + Lorazepam +Clobazam	1	Polytherapy
	Phenytoin + Carbamazepine + Clobazam	1	Polytherapy
	Phenytoin	1	Polytherapy
	Phenytoin + Clobazam	2	Polytherapy
			Monotherapy=7,Polytherapy=10
GTC With Hot Water	Phenytoin + Clobazam	3	Polytherapy
	Phenytoin + Levetiracetam	1	Polytherapy
	Lorazepam + Clobazam	4	Polytherapy
	Clobazam	8	Monotherapy
GTC With Alcohol Abuse	Phenytoin	1	Monotherapy
	Phenytoin + Lorazepam	2	Polytherapy

			Monotherapy=9,Polytherapy=10
Focal Seizures	Phenytoin + Lorazepam	1	Polytherapy
	Lorazepam	1	Monotherapy
			Monotherapy=1,Polytherapy=1

Table 4a: Showing indication wise utilization pattern of drugs and status of poly-therapy of patients. In GTCs which accounts for frequent diagnosis; phenytoin was the 1st drug of choice as monotherapy in 20.45% of cases. However add on therapy with another antiepileptics was introduced for 79.55% of cases along with 1st drug introducing polytherapy. All the time phenytoin and another anti-epileptic drug combination were used as polytherapy except in one case where clobazam and midazolam was also used to treat GTC. Most commonly used add on antiepileptic was lorazepam followed by carbamazepine, phenobarbital, clobazam with phenytoin which introduced polytherapy. At maximum upto 4 different antiepileptic drugs were used to treat different indication. Dugs utilized to treat indications other than GTCs were as shown. Overall the status of polypharmacy was as shown below.

Number of antiepileptic drugs per prescription	Frequency (N)	Percentage (%)	Total
Monotherapy :			
1	43	35.833%	35.833%
Polytherapy :			
2	62	51.66%	64.16%
3	13	10.83%	
4	2	1.666%	
Total =	120	100%	100%

Table 4b: It showed that majority of cases, antiepileptic drugs were used as poly therapy other than monotherapy. Overall 43 (29.86%) patients treated by monotherapy i.e. 1 antiepileptic dugs and 78(63.33%) patients were treated with 2 or more than 2 drugs i.e. polytherapy. Among the patients who got polytherapy, 61 patients got 2 antiepileptics, 13 patients got 3 antiepileptics and 2 patient got 4 antiepileptics drug treatment.

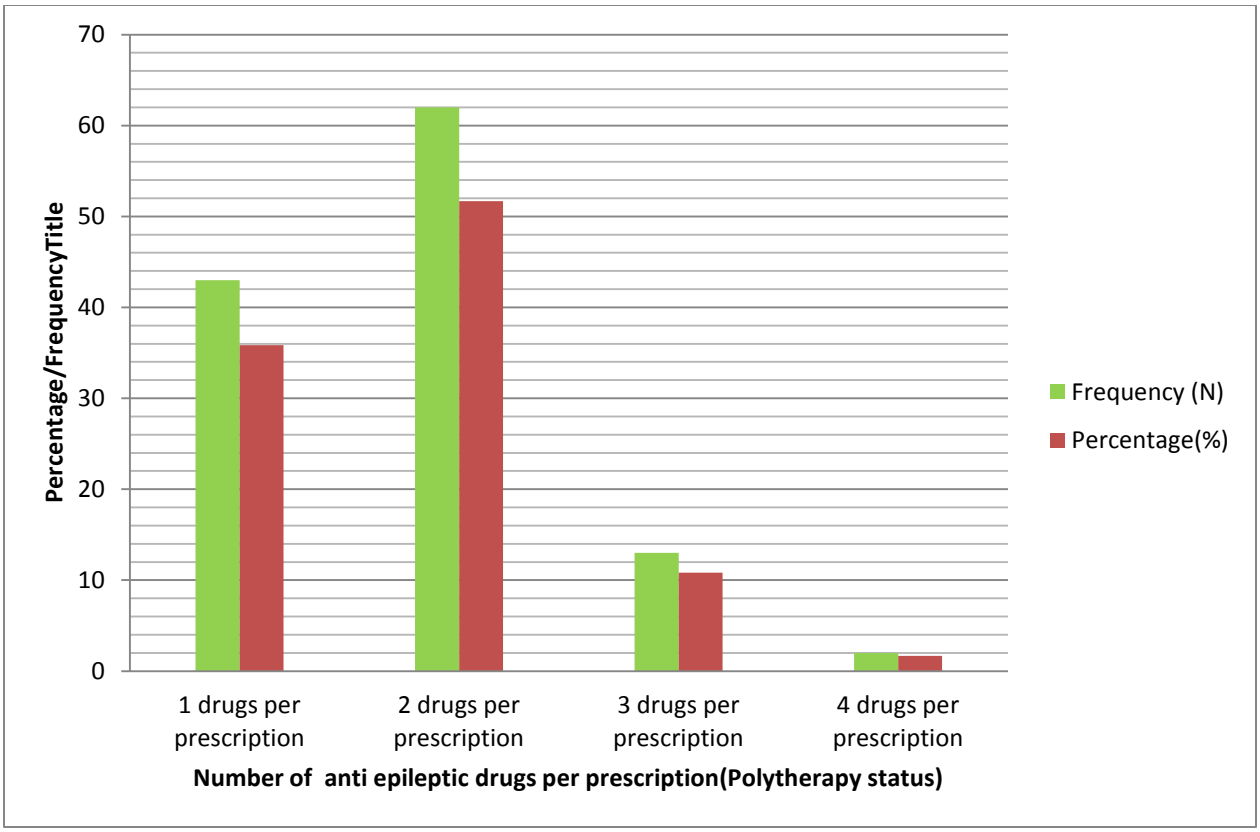


Figure 3: It showed utilization of number of antiepileptic drugs per prescription. Overall polytherapy (64.16%) strategy was used more than monotherapy status (35.833%). 2 drugs per prescription were more than 3 or 4 drugs per prescription respectively.

EXTENT OF ANTIEPILEPTIC DRUG UTILIZATION

Drugs	Frequency (N)	Percentage (%)
Phenytoin	72	34.44%
Carbamazine	17	8.133%
Lorazepam	39	18.660%
Clobazam	48	22.96%
Levetiracetam	7	3.3492%
Phenobarbital	15	7.17%
Midazolam	4	1.91%
Valproic acid	7	3.34%
Total	209	100%

Table No.5: Shows 8 different types of antiepileptic. In 120 prescriptions these drugs were prescribed 209 times. Number of drugs per prescription was 120/209 i.e. 1.74.Extent of utilization of individual drugs in descending order were phenytoin 34.44% followed by carbamazepine 8.133%, lorazepam 18.6%, clobazam 22.96%, levetiracitam 3.34%, phenobarbital 7.17%, midazolam 1.91%, valproic acid 3.34%. Following was the utilization pattern of these drugs presented in figure.

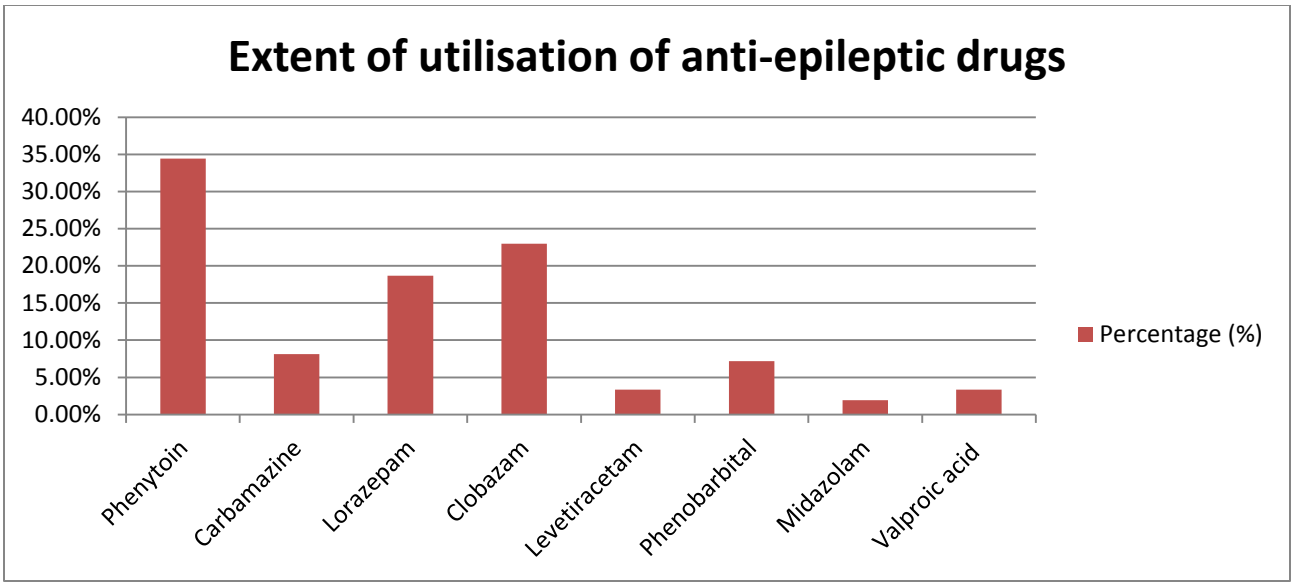


Figure No.4: Extent of utilization of individual anti-epileptics.

GENERATION OF ANTIEPILEPTIC AGENTS

Type of antiepileptic drugs	Frequency(N)	Percentage (%)
Newer generation antiepileptics	8	3.82
Older antiepileptics	201	96.1
Total	209	100

Table No 6: Older Vs Newer generation of antiepileptics. We seen only 1 newer generation antiepileptic agent i.e. levetiracetam which accounts for 3.82% of newer generation antiepileptics in our study. It was used always in conjuction with older antiepileptic drugs as for adjunctive therapy. Remaining 201 i.e. 96.1% of drugs were older generation and they were 7 different types as mentioned in table number 5.

ADVERSE DRUG REACTIONS

ADR and its description	
Drug Name	Carbamazepine
Dose	200 mg
Frequency	Once a day
ADR	Erythema Multiforme Majus.
Age	12
Sex	Female
Naranjo Scale	Probable
Intervention	Accepted and withdrawn of drug immediately
Prevalence	1 out of 17 cases

Table No.7: Out of 120 patients, 17 were exposed to carbamazepine, we had found 1 case of carbamazepine induced erythema multiforme majus.

DRUG - DRUG INTERACTIONS:

TYPE OF DRUG INTERACTIONS

Type of drug interaction	**Frequency (N)**	**Percentage (%)**
Mild	32	39.02
Moderate	14	17.073
Severe	36	43.902
Total	82	100

Table No.8: It showed that that in majority of prescriptions having drug interactions, drug interactions were mostly severe. i.e.36 (30%) which were followed by mild type of interaction 32 (26.66%) and moderate type of interactions14 (11.66%) respectively. Following was the graphical representation of various types of drug interactions.

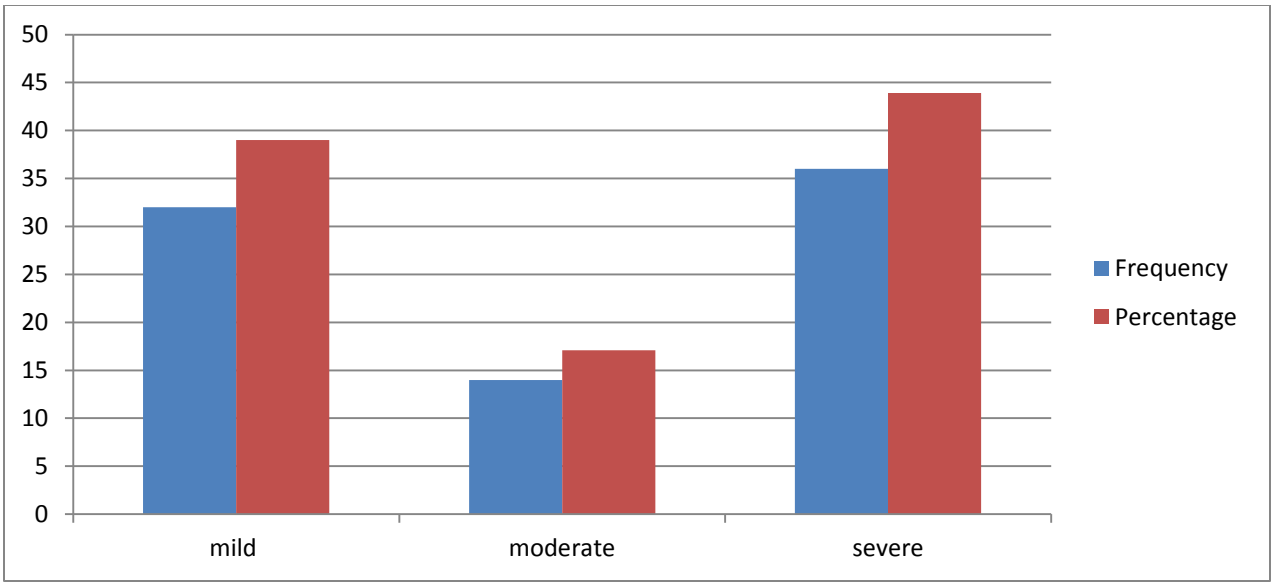


Figure No. 9: Graphical representation of different types of drug interactions.

LIST OF DRUG-DRUG INTERACTIONS

Objective drug	Precipitated drug	Frequency (N)	Percentage (%)
Phenytoin	Metronidazole	2	2.439%
Phenytoin	Phenobarbital	2	2.439%
Ondansetron	Phenobarbital	4	4.878%
Phenobarbital	Lorazepam	3	3.658%
Clobazam	Phenobarbital	4	4.8780%
Albendazole	Phenytoin	3	3.658%
Acetaminophen	Metronidazole	1	1.219%
Calcium gluconate	Amikacin	3	3.65%
Calcium gluconate	Ceftriaxone	3	3.658%
Atorvastatin	Metronidazole	4	4.878%
Vancomycin	Amikacin	3	3.65%

Pantoprazole	Phenobarbital	5	6.09%
Pantoprazole	Clobazam	3	3.65%
Acetaminophen	Lorazepam	5	6.097%
Acetaminophen	Phenytoin	8	9.75%
Atorvastatin	Phenobarbital	4	4.87%
Amikacin	Phenytoin	2	2.43%
Phenytion	Valproic acid	3	3.65%
Carbazepine	Valproic acid	4	4.87%
Valproic acid	Aspirin	1	1.21%
Carbazepine	Pantaprazole	7	8.53%
Lorazepam	Clobaz	3	3.65%
Pantaprazole	Phenytion	2	2.43%
Lorazepam	Alprazolam	2	2.43%
Alprazolam	Phenobarbitone	1	1.21%
Total drug interaction		82	100%

Table No.9: It showed that out of 120 prescriptions, 82 different drug-drug interactions were identified. Most commonly (9.75%) we seen acetaminophen plus phenytoin were interacting. Other different drug interactions were as shown in table.

MECHANISM OF DRUG - DRUG INTERACTIONS

Mechanism of drug interaction	Frequency (N)	Percentage (%)
Pharmacokinetics drug interactions	66	80.4878
Pharmacodynamic drug interactions	4	4.878049
Both	12	14.63415
Total	82	100%

Table No.10: It showed that majority of patients were having drug interaction by pharmacokinetic mechanisms i.e. 66(55%) followed by both pharmacokinetic and pharmacodynamic mechanism 12 (10%) and pharmacodynamic mechanisms 3(2.5%).

MEDICATION ADHERENCE BEHAVIOR:

Medication Adherence Level (scale)	Number of patients (N)	Percentage (%)
High adherence (0)	25	20.83%
Medium adherence (1-2)	15	12.5%
Low adherence (3-8)	80	66.66%
Total	120	100%

Table No. 11: It showed that among 120 patients majority of patients (66.66%) were having low adherence behavior (3-8) for medication whereas only 20.83% of patients were having high (0) adherence behavior in baseline. Consequently 12.5% of patients were having moderate (1-2) type of adherence Following was the level of adherence represented in figure.

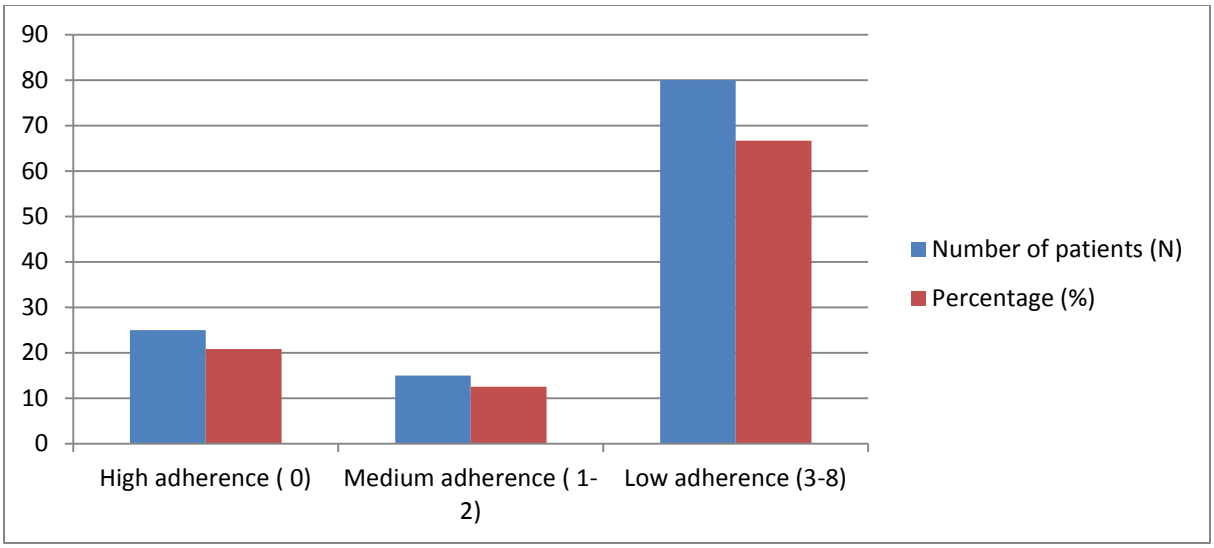
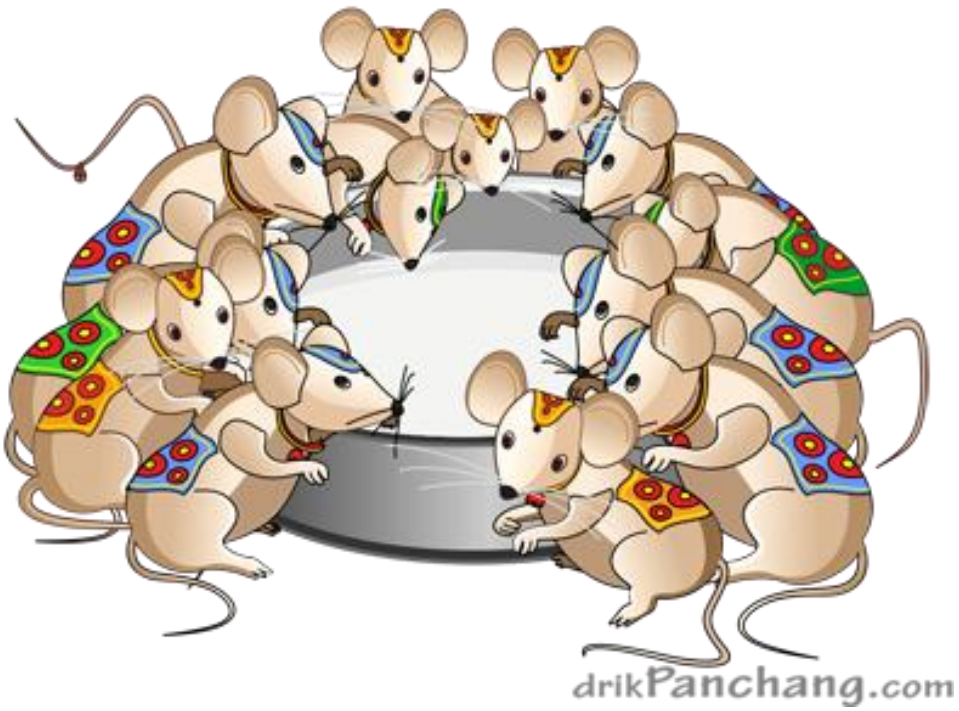


Figure No 10: Level and Score of medication adherence behavior of patients in MMAS-8 Questionnaires.

CLINICAL PHARMACIST MEDIATED INTERVENTIONS IN NUT SHELL

Clinical pharmacist service provided	**Drug related problems**	**Notified to physician**	**Physcian Acceptance**	**Action taken**
Identification of Drug interaction	Severe drug interaction	Yes	Yes	Monitoring of clinical effects
	Moderate drug interaction	Yes	Yes	Not taken
	Mild drug interaction	Yes	Yes	Not taken
Identification and ADR monitoring	Reversible carbamazepine induced rashes	Yes	Yes	Drug Withdrawn
Patient counselling	Low medication adherence level	Yes	yes	Patient counselling provided by clinical pharmacist

Table No.12: It showed that all the drug related problems either potential or actual were notified to physician where all got accepted but only in cases of severe drug interaction, low medication adherence and adverse drug reaction further action was taken.



Discussion

This study provides the insights of current trend of antiepileptic drugs utilization pattern in rural tertiary care teaching hospital.

DEMOGRAPHIC DETAILS OF PATIENTS

GENDER DISTRIBUTION

Among 120 patients studied; we seen female (N=70, 58.33%) were predominant than males (N=50, 41.66%). In contrast to our results; Murthy NV et al showed males were more frequently attacked with epilepsy than females.[7] It is however that T.Badwaik et al seen females were more than males in their study exposed to antiepileptic drugs, which complements our result.[48]

AGE DISTRIBUTION

In our study we frequently found more pediatric (70) cases i.e., age group less than 18 years than adults (50) cases. From medicine units most patients were between 36-60 age groups. According to the literatures, the incidence of epilepsy has a bimodal distribution with a peak in the first decade and a second peak in the elderly and our result is in accordance with it. [55, 56, 57]

DIAGNOSIS AND CO-MORBIDITIES

Most frequent diagnosis in our study was epilepsy without any co-morbidity which accounts for 80% of diagnosis. It tells that epilepsy due to co-morbidities are less in our study. Generalized tonic clonic (GTC) seizure was the most common type of epilepsy. This result is similar to studies from Akinsulore A et al and Murthy NV et al where they also seen GTCs as a major diagnosis.[7,39] Rest of the 20% of diagnosis were associated with co-morbidities like both diabetes and hypertension, meningitis, cardiovascular accident, alcohol withdrawal syndrome, viral fever, migraine, and bronchopneumonia. Junny Sebastian et al also seen hypertension as most

common comorbidity like our study,[30] but always it will not be the same case. Study from Germany found cerebrovascular accident, dementia, and intra cerebral hematoma as a most common comorbidities.[58]

TYPES OF EPILEPSY

In our hospital most patients were suffering from generalized tonic clonic seizures during this period followed by atypical seizures, typical seizures, status epilepticus, febrile seizures, partial seizures, generalized tonic clonic seizures by alchohol dependence and by hot water and febrile seizure. A study from Mysore, south India also seen similar pattern of epilepsy.[30]

DRUG UTILISATION EVALUATION OF ANTIEPILEPTIC DRUGS

There are above 20 antiepileptic drugs which are available for clinical use today. In our hospital only 8 different antiepileptic drugs were used however. In 120 prescriptions; 209 were antiepileptic drugs and 163 non antiepileptic drugs. This study highlighted that Phenytoin was the most commonly prescribed antiepileptic drug. Similar results were obtained by Sobhana et al.[58] Recently published studies (2002- 2013) mention that sodium valproate was the most commonly drug prescribed followed by phenytoin or other drugs.[7,49,60,61,62] We seen very less prescription for this drug however (3.34%). An Indian study by Thomas SV et al 2001 mentioned that carbamazepine was prescribed most commonly.[63] Comming into the lesser side we had seen very less prescription for drugs like midazolam and levetiracetam. This shows the existing of wide variation of prescribing in antiepileptic drugs. The reason for discrepancies may be due to factors like availability, affordability, place of practice, type of epilepsy and preference of treating neurologist etc. Phenytoin is broad spectrum antiepileptic most commonly used for partial onset seizure as well as generalised clonic tonic seizures. Being cheap, it is also widely

available, which enhances its use in our set up of tertiary care hospital. We also found some non-antiepileptic drugs prescribed due to different co-morbidities. Most common was non steroidal anti-inflammatory drugs followed by antibiotics, antidiabetics, H2 receptor antagonist etc. Due to these con-current drugs we found potential drug-drug interactions with antiepileptic agents. We also seen that 90 % of prescriptions were containing at least one parenteral formulation and 10 % of prescriptions were containing oral formulations. We had also seen that varying number of dosage forms in prescriptions. i.e from 1 dosage form in a prescription to 4 different dosage forms. If there are different types of dosage forms prescribed for a patient, patient counseling especially about administer technique is needed to increase compliance. For example in some cases suppositories, tablets, syrups, injections were prescribed for same patient. In our setting there were no clinical pharmacists to provide such service. We also witnessed the fact that majority of patient are not aware of how to administer different dosage forms.

INDICATION WISE USE OF ANTIEPILEPTIC DRUGS

Drug therapy is the mainstay of epilepsy treatment. The choice of antiepileptic drugs will depend on types 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 but all are not seizure free.

In GTCs which accounts for frequent diagnosis; phenytoin was the 1st drug of choice as monotherapy in 20.45% of cases. However add on therapy with another antiepileptics was introduced for 79.55% of cases along with 1st drug introducing polytherapy. All the time phenytoin and another anti-epileptic drug combination were used as polytherapy except in one case where clobazam and midazolam was also used to treat GTC. Most commonly used add on

antiepileptic was lorazepam followed by carbamazepine, phenobarbital, clobazam with phenytoin which introduced polytherapy. At maximum upto 4 different antiepileptic drugs were used to treat different GTCs. These all things highlighted the fact that to treat GTCs, still traditional approach of using phenytoin/Phenobarbital was continued. Carbamazepine and valproic acids also have equal efficacy and fewer side effects and can be preferred. dipiro. Carbamazepine is considered an AED of first choice for newly diagnosed partial seizures and for primary GTC seizures that are not considered an emergency whereas valproic acid is also indicated to treat mixed seizure disorders. No newer antiepileptics as adjunctive therapy was noted. We also found considerable difference in therapy to treat GTCs caused by hot water and alcohol abuse. Clobazam as a monotherapy, and lorazepam plus clobazam as polytherapy was used commonly to treat hot water GTCs. However to treat alcohol abuse related GTCs, phenytoin plus lorazepam combination was used most commonly. In typical seizure monotherapy with clobazam was preferred choice however if they required polytherapy they were tried with Phenobarbital as adjunct to clobazam. Some cases of typical seizures were treated with combination that started with phenytoin as a monotherapy. Similarly in febrile eizures most commonly carbamazepine was used rather than phenytoin. To treat status epileptics phenytoin and its combination with other antiepileptic like lorazepam, Phenobarbital, levetiracetam and midazolam was used. Maximum of upto 4 drugs were used. Similarly to treat partial seizures levetiracetam and carbamazepine as monotherapy was used. Focal and atypical seizure there was high use of phenytoin.

Based on these findings we highlighted that phenytoin was mostly used. Phenytoin was not used to treat febrile seizures. Carbamazepine was used in these cases. Levetiracetam was used as monotherapy as well as in combination with carbamazepine to treat focal seizures only.

Valproate was used as adjunctive therapy in different types of epilepsy including status epilepticus. Clobazam was used as monotherapy specially to treat hot water epilepsy and with different indication as polytherapy. Lorazepam alone was never used but only in combination it was used. Phenobarbital was not used in partial, atypical, focal seizures but when used it was utilized as adjunctive therapy to treat other indications. Midazolam was used in case of just GTCs and status epilepticus as adjunctive therapy.

MONOTHERAPY VS POLYTHERAPY.

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 our study we found that 35.83% of the patients were on monotherapy and 64.16% were on polytherapy i.e. > 2 or more antiepileptic drugs. These results are not in conjuncture with other studies.[7, 59, 49, 61] where they found that most of the patients (≥50%) were prescribed single drug. 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.[65] In our study upto 4 different antiepileptic drugs were prescribed in a prescription at maximum but poly therapy by two antiepileptics were most common. This may be due to the fact of failing of monotherapy or using polytherapy by physician at once in severe or life threatening situation. Failing of monotherapy may also result from lack of adherence resulted from no proper counseling about their medication to the rural patient. It is found that up to 60%

of patients with epilepsy are noncompliant, and this is the most common reason for treatment failure.[35]

UTILISATION OF NEWER VS OLDER ANTIEPILEPTICS

Drugs introduced before 1990's are called older and after 1990's are newer antiepileptic drugs. We found very less new antiepileptic drugs than older ones in prescriptions. This is similar to studies performed in India highlighted the limited use of newer antiepileptics drugs.[49] Guidelines for the management of epilepsy in India, 2013 shows that newer antiepileptic drugs and their discovery has not altered treatment regimen.[64] However it has increased treatment choice in refractory cases. So far, no studies have shown that the newer drugs have superior anticonvulsant efficacy than older ones but have favorable side effects. Less use in our settings may also be due to higher cost of these agents compared to older ones. In our study we found Levetiracetam as only one newer antiepileptic and older ones include Carbamazepine, Phenytoin, Valproate, Clobazam, Lorazepam, Phenobarbital and Midazolam. Most commonly polytherapy include two drugs per prescription other than 3 drugs per prescription and 4 drugs per prescription.

ADVERSE DRUG REACTION

A Female of 12 years of age took Carbamazepine 200 mg O.D for partial seizure and after 2 days she developed skin rashes all over the body .It was identified as erythema multiforme majus.The reaction was a Type B based on Rawlins and Thompson classification. According to Naranjo scale and WHO scale and it was probabale ADRs. We notified this adverse drug reaction to attending physician. The intervention was accepted and drug was tapered before withdrawn .They added levetiracetam 10 mg once daily. Due to this adverse drug reaction patient got 1 more day of hospitalization was observed. This reaction with carbamazepine occur 1-2 every

100,000 patient population. In our study we seen this reaction out of 17 patient exposed to this drug. This reaction mimics steven johonson and toxic epidermal necrosis which can also occur by this drug. However this reaction is characterized by erythema and moderate to extensive scaling of involvement of total or near total body surface. Upto now no patient had died due to this reaction and is not severe.[65] The adverse drug reaction was reversible as rashes disappeared upon discontinuation.

DRUG INTERACTIONS

Drug interaction determines the safety aspects of drug use. Clinically it can be classified as mild, moderate and severe whereas based on the mechanism; it can be divided into pharmacokinetic and pharmacodynamic interactions.[66] We seen different antiepileptic drugs interacting with both antiepeileptic drugs and also with other drugs used for co-morbidities. As in our study majority of drugs are older generations they have high chance of interaction. In therapeutics, these classes of drugs are mostly interacting drugs.[35] Drug-drug interaction among antiepileptic drugs can happen due to refractory cases of epilepsy requiring polytherapy and use of antiepileptic drugs for multiple indications etc, [66] in our study. The potential for interactions with other drugs increase with increasing age, and the elderly is the largest group with new onset epilepsy having a considerable risk of interactions with commonly prescribed drugs etc.[67]

TYPE AND MECHANISM OF DRUG INTERACTION

In our study we found more cases of severe type of drug interaction followed by mild and moderate cases. All these interactions were potential interactions. There are two mechanisms by which drug-drug interaction may take place. They are pharmacodynamic and pharmacokinetic mechanism. Pharmacodynamic interactions are those which occur at the drug's site of action and

do not involve change in plasma drug concentrations but alter i.e attenuate or enhance efficacy and adverse effects. There was very less amount of such interaction in our setting. Most commonly we saw pharmacokinetic drug interaction. In general, pharmacokinetic interactions may alter absorption, protein binding, metabolism, and excretion of any drug, They are usually related to alterations in metabolism by enzyme inducers or inhibitors. Enzyme induction involves the synthesis of new enzyme, requires protein synthesis and may take many days before it is completed, resulting in increased metabolism, decreased serum concentrations and pharmacological effect (if no active metabolites are present) of the affected drug, and possibly loss of seizure control. Enzyme inhibition results from competition between drugs for the same active site on the enzyme and results in decreased metabolism of the affected drug. Circulating concentrations of the inhibited drug increase to a new steady-state about five half-lives after the interaction. Consequently, pharmacological potentiation will occur quickly if the drug has a short half-life and more slowly if it has a long half-life (20-23). In our study we found 80% of drug interactions were pharmacokinetic, 4.87% of drug interaction were pharmacodynamic and 14% were both pharmacokinetic and pharmacokinetic. Our study highlighted that mostly drug interaction will occur through pharmacokinetic interaction.

DIFFERENT INTERACTING DRUGS

Among 82 potential drug interactions we seen 8 different interactions were having both antiepileptic drugs and rest of them (74) were having interaction with other drugs used for co-morbidities. Phenobarbital was mostly interacting with number of other drugs possibly through enzyme induction. Likewise Carbamazepine plus Pantoprazole accounted for frequently encountered drug interaction in our settings.

MEDICATION ADHERENCE BEHAVIOR OF PATIENT

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.[72] Adherence level of patient will focus on patient's drug related problems which can be resolved. In epilepsy patient they have to take medications for years. So to observe medication adherence behavior to this patient useful. Medication adherence can be assessed by either indirect or direct methods. Direct methods to measure adherence are attendance to direct observed therapy and measurement of the level of medication or metabolite and biological markers in the blood.[72] 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. We used patient self reporting indirect method to assess medication adherence by validated MMAS-8 questionnaires. This questionnaire consist 8 questions where 0 is given to answer 'Yes' and 1 is given to answer 'No' from question 1 to 7 where 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).

The prevalence of self-reported poor adherence to AED therapy among our study subjects is poor and is contrast to those reported in previous studies of the western population.[72] Very high level of non adherence has also been reported from Malaysia.[74] In 2003, WHO reported that the prevalence of adherence to AEDs in developing countries ranged between 20% and 80%. 26 Hence, our finding showed that the issue of poor adherence is not changing in India. As we found 66.66% of patient were having low adherence and 12.5% of patient were having medium

level of adherence. These were the poor adherence groups. So we counseled them to improve further of their medication adherence behavior. Base line follow up to see the outcome however was not done.

These patient who were having poor adherence, may had multiple reason for this.[72] In younger age patients; medication taking behavior will depend on their care takers. Care takers have to make counseled regarding medication use. This is not happening because there is high workload of physician for medication related counseling and no patient counseling service provided by other health care professionals in our settings. Care takers and patient themselves are will not be aware to seek proper medication advice. Poor understanding about the nature of, and need for the AED therapy could lead to poor adherence level. In these instances patients will realize the benefits of adherence only as time passed because they learn from their personal experience.[73] WHO also reported that patients with busy lifestyles commonly do not adhere to medication.[75] but this was not the common reason in our settings. Very interestingly one study reported that more than half of the epilepsy patients thought that they could reduce or cease taking the AEDs just to see what would happen.[76] So there may be multiple reasons existing for non adherence. Our study indicates that health care professionals should spend sufficient time in educating the patients to improve the adherence level especially for newly diagnosed and younger epilepsy patients as majority of people were having poor adherence level.

CLINICAL PHARMACIST MEDIATED INTERVENTIONS IN NUT SHELL

Drug related problems can be potential and actual. Potential are those which will happen in near future but actual drug related problem are those which was already happened. All drug interactions in our study were potential. ADR and low adherence level were actual drug related problems. These problems were all notified to the respective physician. They accepted all these

problems but only in cases like ADR and severe drug interaction further action were taken. Drug was withdrawn immediately in case of ADR but in case of some drug interactions they monitor clinical effect. In all patients having low to moderate adherence level we counseled the patient regarding disease and medication. We highlighted the role of clinical pharmacist in this research work by identifying and resolving drug related problems. We want to conclude that physician acceptance of clinical pharmacist role is increasing in our hospital.

Conclusion

Based on the results we would like to conclude that

- Prescribing pattern of antiepileptic drugs shown very less prescriptions for newer antiepileptic drugs. Only one drug i.e. Levetiracetam was used. Newer antiepileptic drugs can be tried in practice as indicated because they have less side effects

- Most commonly phenytoin was utilised. This is enzyme inducing drug and will show non linear pharmacokinetics. So Therapeutic drug monitoring is essential.

- Polyptherapy in prescriptions is more than monotherapy and majority of patients were having low medication adherence. Patient counselling service is needed which can improve the patient medication taking behaviour.

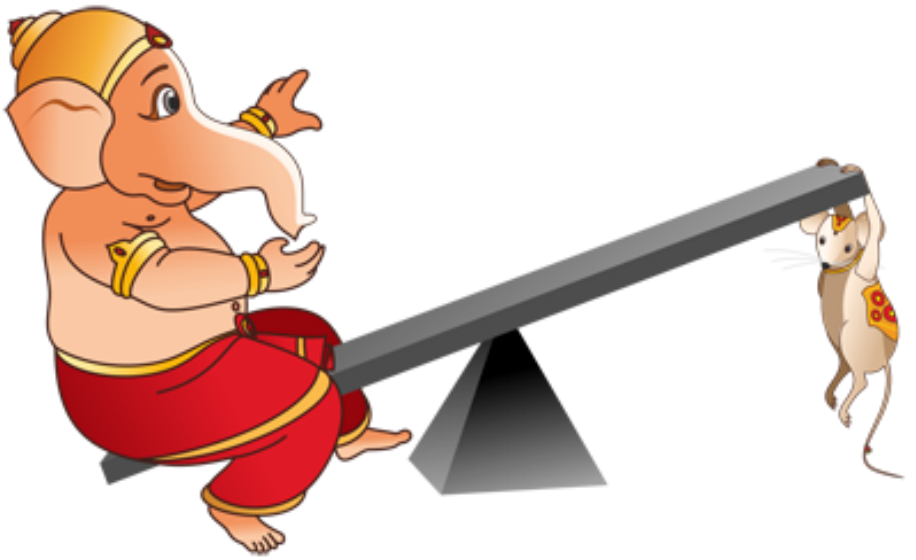
- Because of co-morbidities; antiepileptic drugs have smore chance of interaction with other drugs. So before prescribing other drugs we have to check this drug interaction. Clinical pharmacist mediated drug interaction monitoring service will be useful in this regard.

- Because ADR incidence of antiepileptic drug is high, ADR identification and reporting has to be encouraged to nurses, physician and even to the patients.

Summary

A prospective observational hospital based study was carried out for 9 months in 120 in-patients who were admitted to medicine and pediatric department of AH and RC, BG Nagara.

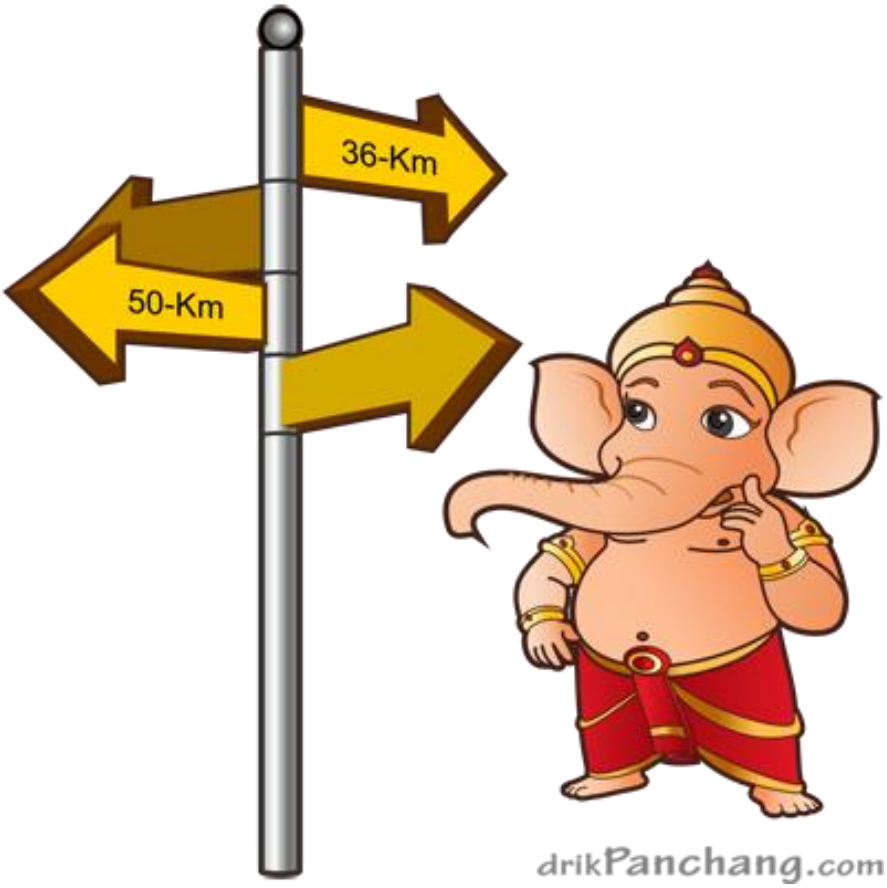
- ✓ Female (58.33%) patient were more than male (41.66%) patients and majority (58.33%) of patients were under age group of 0-18.
- ✓ Generalized tonic clonic epilepsy (36.66%) was the most common type of epilepsy followed by typical (14.15%), febrile seizures (13.3%) status epilepticus (7.5%) and partial seizure (4.16%).
- ✓ Most commonly prescribed drug was Phenytoin (34.44%), Clobazam (22.96%), lorazepam (18.66%), carbamazepine (8.13%), Phenobarbital (7.17%), Levetiracetam (3.34%), valproic acid (3.34%) and midazolam (1.9%).
- ✓ Very less number of newer antiepileptic (3.82%) agents was used in compared to older ones (96.1%).One drug namely Levetiracetam is only used as adjunct therapy but not as monotherapy.
- ✓ Prevalence of polytherapy is high (64.16%) compared to monotherapy.
- ✓ Out of 37 patient exposed to carbamazepine we found one adverse drug reaction of carbamazepine induced rashes.
- ✓ Chance of occurring severe drug interactions (43.12%) were more other than moderate (17.073%) and mild case (39.02%) which is a big problem. Most commonly phenytoin was interacting with acetaminophen.
- ✓ On MMAS-8 questionnaire scale 66.66% patients showed low adherence level followed by high adherence (40.8%) and medium (12.5%) level of adherence.
- ✓ We notified drug therapy related issues to physician. All interventions were accepted and welcomed by physicians. Majority of cases action were taken. In case of patient having low medication adherence, we counseled them.



Limitations

LIMITATIONS

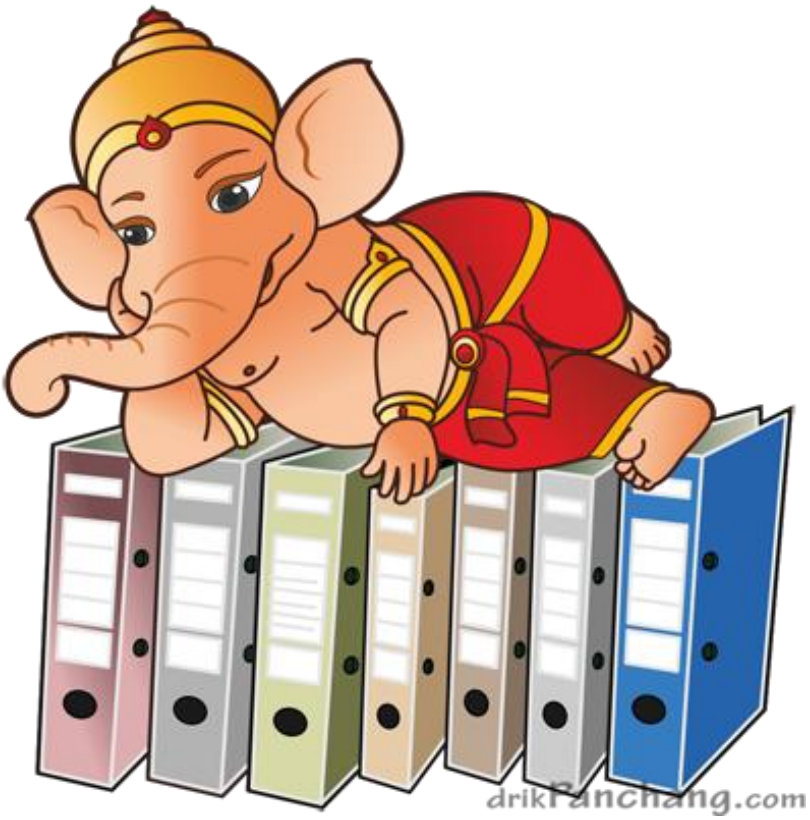
- The study can be conducted in large population in multiple centers.
- A pediatric and medicine patients visiting outpatient were not included.
- Pregnant/lactating women and psychiatric patients were not included in this study.
- The study requires longer duration of followings with more number of prescriptions.



Future Directions

FUTURE DIRECTION

- Similar study can be carried out in an out-patients paediatrics and medicine departments also.
- Safety and efficacy of medications can be studied comparatively as separate research in Pediatric patients.
- Pharmacoeconomic study can be done.
- The DUE study can be conducted for longer period.
- Study can be conducted in a community pharmacy setup by educating the patients suffering from chronic diseases for the benefit of patients.



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Annexures

PATIENT CONSENT FORM

I …… (patient/Guardian) have been explained by the investigators Mr. M. Kumaraswamy / Miss. Sharvani. H. About the study entitled "A study on drug utilization pattern of anti - epileptic drugs in rural tertiary care teaching hospital"

I am Patient/guardian (if patient is below 18 years of age) here by give the consent to be included as a participant in this study.

1. I have been explained about the nature of the study.
2. I have informed the investigator of all the treatments I am taking or have taken in the past months including any alternative treatments.
3. I have the option to withdraw from the trial at any stage.
4. I have been answered to my questions by the investigator about the study.
5. I have decided to be in the research study.

I am aware, that if I have any questions during this study, I should contact at any of the above investigators.

Date:

Place:

Name of patient/guardian:

Thumb impression/Signature:

Signature of Investigators:

|| Jai Sri Gurudev ||
Sri Adichunchanagiri Shikshana Trust (R)
Adichunchanagiri Institute of Medical Sciences
(Recognised by Medical Council of India, New Delhi, General Medical Council,
London (U.K.) &Affiliated to Rajiv Gandhi University of Health Sciences, Karnataka)

No. AIMS/IEC/105/2015-16 Date: 24-08-2015

CERTIFICATE

This is to certify that the M.Pharm research project titled " A study on drug utilization pattern of antiepileptic drugs in rural tertiary care teaching hospital" to be conducted by the research scholars Ms Sharvani Hugara (Reg no 14PR006) under the guidance of Mr M Kumaraswamy, Associate Professor, Department of Pharmacy practice, Sri Adichunchanagiri College of Pharmacy has been discussed and approved by the Institutional Ethical Committee, Adichunchanagiri Institute of Medical Sciences, BG Nagara, Mandya dist., Karnataka - 571448 in the meeting held on 24th August, 2015.

Member Secretary
IEC, AIMS, BG Nagara

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"ಜೈ ಶ್ರೀ ಗುರುದೇವ್"

ಶ್ರೀ ಆದಿಚುಂಚನಗಿರಿ ಔಷಧ ವಿಜ್ಞಾನ ಮಹಾವಿದ್ಯಾಲಯ
ಕ್ಲಿನಿಕಲ್ ಫಾರ್ಮಸಿ ಡಿಪಾರ್ಟ್‌ಮೆಂಟ್
ಶ್ರೀ ಆದಿಚುಂಚನಗಿರಿ ಆಸ್ಪತ್ರೆ ಮತ್ತು ಸಂಶೋಧನಾ ಕೇಂದ್ರ
ಬಿ.ಜಿ.ನಗರ–571448.

ರೋಗಿಯ ಸಮ್ಮತಿ ಪತ್ರ

ನಾನು _____ (ರೋಗಿಯು/ಪಾಲಕರು 18 ವರ್ಷದ ಒಳಗಿನ ಮಕ್ಕಳಿದ್ದರೆ) ಈ ಕೆಳಗಿನ ಅಧ್ಯಯನವಾದ **"ಗ್ರಾಮೀಣ ತೃತೀಯ ಆರೈಕೆ ಬೋಧನಾ ಆಸ್ಪತ್ರೆಯಲ್ಲಿ ಮೂರ್ಛೆರೋಗಕ್ಕೆ ಬಳಸುವ ಔಷಧಗಳ ಉಪಯೋಗ ಮತ್ತು ಮಾದರಿಯ ವಿಮರ್ಶನೆ"** ಬಗ್ಗೆ ಅಧ್ಯಯನಕಾರರು ನನಗೆ ಸಂಪೂರ್ಣವಾಗಿ ತಿಳಿಸಿರುತ್ತಾರೆ.

- ನನಗೆ ಈ ಅಧ್ಯಯನದ ರೀತಿಯನ್ನು ತಿಳಿಸಿರುತ್ತಾರೆ.
- ಹಿಂದೆ ತೆಗೆದುಕೊಂಡಿರುವ ಮತ್ತು ತೆಗೆದುಕೊಳ್ಳುತ್ತಿರುವ ಔಷಧಗಳ ಬಗ್ಗೆ ಅಧ್ಯಯನಕಾರರು ಸಂಪೂರ್ಣ ವಿವರ ತಿಳಿದಿರುತ್ತಾರೆ.
- ನಾನು ಅಧ್ಯಯನಕಾರರಿಂದ ಅಧ್ಯಯನದ ಸಮಸ್ಯೆಗಳಿಗೆ ಉತ್ತರ ಕಂಡುಕೊಂಡಿರುತ್ತೇನೆ.
- ನಾನು ಯಾವ ಕ್ಷಣದಲ್ಲಾದರು ಈ ಅಧ್ಯಯನದಿಂದ ಹೊರನಡೆಯಬಹುದೆಂದು ತಿಳಿದಿರುತ್ತೇನೆ.
- ನಾನು ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗಿ ಆಗಬೇಕೆಂದು ನಿರ್ಧರಿಸಿದ್ದೇನೆ.

ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗಿಯಾಗಿರುವಾಗ ನನಗೆ ಯಾವುದೇ ಗೊಂದಲಗಳು ಬಂದಲ್ಲಿ ಅದನ್ನು ಈ ಮೇಲಿನ ಅಧ್ಯಯನಕಾರರಿಂದ ಬಗೆಹರಿಸಿಕೊಳ್ಳುತ್ತೇನೆ.

ರೋಗಿಯ ಹೆಸರು: ರೋಗಿಯ ಸಹಿ/ಹೆಬ್ಬೆಟ್ಟಿನ ಗುರುತು

ದಿನಾಂಕ:

ತನಿಖೆದಾರರ ಸಹಿ:

©Morisky Medication Adherence Scale (MMAS-8-Item). This is a generic adherence scale and the name of the health concern can be substituted in each question item.

You indicated that you are taking medication(s) for your (identify health concern, such as "high blood pressure"). Individuals have identified several issues regarding their medication-taking behavior and we are interested in your experiences. There is no right or wrong answer. Please answer each question based on your personal experience with your [health concern] medication.

(Please mark your response below)

	No=1	**Yes=0**
1. Do you sometimes forget to take your [health concern] medication(s)?		
2. People sometimes miss taking their medications for reasons other than forgetting. Thinking over the past two weeks, were there any days when you did not take your [health concern] medication(s)?		
3. Have you ever cut back or stopped taking your medication(s) without telling your doctor, because you felt worse when you took it?		
4. When you travel or leave home, do you sometimes forget to bring along your [health concern] medication(s)?		
5. Did you take your [health concern] medication(s) yesterday?		
6. When you feel like your [health concern] is under control, do you sometimes stop taking your medication(s)?		
7. Taking medication(s) every day is a real inconvenience for some people. Do you ever feel hassled about sticking to your [health concern] treatment plan?		

8. How often do you have difficulty remembering to take all your medication(s)?

(Please circle your answer below)

Never/Rarely……....**4**

Once in a while……**3**

Sometimes……....**2**

Usually……**1**

All the time……..**0**

II Jai Sri Gurudev II

Sri Adichunchanagiri College of Pharmacy

Department of Pharmacy Practice

Adichunchanagiri Hospital and Research Centre, B.G.Nagara-571488

PATIENT DATA COLLECTION FORM

RESEARCH TITLE: "A STUDY ON DRUG UTILIZATION PATTERN OF ANTIEPILEPTIC DRUGS IN RURAL TERTIARY CARE TEACHING HOSPITAL"

PATIENT DETAILS:

Name: Age: Gender: M / F Weight:

IP/OP No: Department/Unit: DOA: DOD:

OCCUPATION: (Parents occupation if patient below 18 years)

Employed ☐ Unemployed ☐ Farmer ☐ Business ☐

EDUCATION; Primary ☐ Secondary ☐ SSLC ☐ Above SSLC ☐

REASONS FOR ADMISSION:

MEDICAL AND MEDICATION HISTORY:

FAMILY HISTORY:

LAB INVESTIGATIONS:

Electroencephalography(EEG) scan:

Brain scan-MRI/CT scan:

Blood test:

Electrolyte test: Na^+:
K^+:
Cl^-:

OTHERS:

FINAL DIAGNOSIS:

DRUGS TREATMENTCHART WITH DOSE, DOSAGE FORM&ROUTE		Dose	Route	Frequency	Dosage form	Starting Date	stopped date	Indication of drug
S.N	GENERIC NAME							

IS THERE ANY POLY PHARMACY: Yes ☐ No ☐

☐ 2-5 ☐ 5-10 ☐ More than 10 drugs

IS THERE ANY DRUG INTERACTION IDENTIFIED? ☐ Yes ☐ No

Documentation: Mild/ Moderate/ Severe.

Nature of interaction

☐ Drug-drug interaction ☐ Drug-food interaction.

☐ Drug-lab interaction ☐ Others.

Type of interaction

☐ Pharmacokinetic interaction

☐ Pharmacodynamic interaction

Intervention done: Yes ☐ No ☐

Sl no	Obj

ADVERSE DRUG REACTION IF ANY:

Is there any adverse drug reaction identified? ☐ Yes ☐ No

ADR assessment scales :

WHO Scale:

☐ Certain ☐ Probable ☐ Unlikely ☐ Possible ☐ Conditional ☐ Unassessible

Naranjo scale score:

☐ Definite ☐ Possibly ☐ Probable ☐ Unlikely

Intervention done: Yes ☐ No ☐

Drugs	Events description	Management	Out come
		☐ Close monitoring ☐ Continue with small dose ☐ Discontinue ☐ Discontinue and treat ADR	Cured Not cured

Name and Signature of the student:

……

Signature of the Guide:

...……