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**Research Article**

# DRUG USE EVALUATION OF ANTIEPILEPTIC DRUGS IN OUTPATIENT EPILEPSY CLINIC OF BISHOFT GENERAL HOSPITAL, EAST SHOA, ETHIOPIA

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## ABSTRACT

**Background:** Epilepsy, a chronic condition defined as two or more recurrent, unprovoked seizures, which has the highest incidence at the end of life. Antiepileptic drugs (AEDs) are primary therapeutic mode for epilepsy. AED treatment has been demonstrated to control seizure, which decreases morbidity and mortality associated with epilepsy. Nevertheless, the risks of significant adverse effects and drug interaction increase when more than one drug is used. Hence, drug use evaluation (DUE) programs play a key role in helping managed health care systems understand, interpret, and improve the prescribing, administration, and use of AEDs.

**Objective:** The purpose of this study was to evaluate use of antiepileptic drugs in epilepsy Outpatient Clinic of Bishoftu General Hospital (BGH), East Shewa, Ethiopia.

**Method:** 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.

**Result:** 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, 172 and 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 indication set 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%.

**Conclusions and recommendations:** 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.

**Keywords:** Drug use Evaluation, Epilepsy, AEDs, Drug utilization, Seizure.

## INTRODUCTION

Epilepsy is a major public health concern, directly affecting an estimated 50 million people worldwide and involving an additional 500 million people as family members and caregivers of patients. The Atlas of Epilepsy care, which was published in 2005 jointly by the world Health organization (WHO), the International League against Epilepsy (ILAE) and the International Bureau for Epilepsy (IBE), describes global dimensions of epilepsy, and highlights the difficulties encountered in implementing epilepsy care programs (1).

Epilepsy is a chronic disorder characterized by recurrent seizures (2). It is estimated that there are 5,500,000 persons with epilepsy in India, 2,000, 000 in USA and 300,000 in UK (3). Ethiopia is among those sub-Saharan countries

affected by epilepsy chronic neurological disease. In Ethiopia the annual incidence of epilepsy is 64 in 100,000 in habitants (4).

The general approach to treatment involves the identification of goals, assessment, development of a care plan and a follow-up evaluation. During the assessment phase, it is critical to establish an accurate diagnosis of the seizure type and classifications (5). The diagnosis of epilepsy is essentially clinical, based on an eyewitness account of the seizure. Neurological examination and investigations may be normal between attacks; Sometimes patients may not be aware of the nature of attacks; seizures occurring at night may go unnoticed. Patients with infrequent or mild seizure may not receive ongoing medical care and so may be missed. Patients may also tend to deny a history of epilepsy in view of the stigma, attached to it or feign epilepsy (6).

The choice of the most appropriate drug treatment for a patient with seizures depends upon the accurate classification of the seizures, the type of epilepsy or epileptic syndromes, and drug such as availability and accessibility, efficacy, side effect profile and ease of use as well as patient factors. The aim of therapy is to minimize the recurrence of the seizures and the adverse drugs. Over 80% of epileptic patients can achieve a significant reduction in seizure frequency with one drug alone (7). The ultimate goal of treatment for epilepsy is no seizure and no side effects with an optimal quality of life. The best quality of life is associated with a seizure free state (8).

Drug utilization was defined in 1977 as "the marketing, distribution, prescription and use of drugs in a society, with special emphasis on the resulting medical, social and economic consequences" (9). Drug use evaluation (DUE) was originally known as drug utilization review (DUR) in the 1970s and early 1980's. The term drug utilization review (DUR) and drug use evaluation (DUE) is interchangeable (10). DUE is an ongoing, systematic process designed to maintain the appropriate and effective use of drugs. It involves comprehensive review of patients' prescription and medication data before, during and after dispensing in order to assure appropriate therapeutic discussion making and positive patient outcomes. Pharmacists participating in DUE programs can directly improve the quality of care for patients, individually & as populations, by preventing the use of unnecessary or inappropriate drug therapy & by preventing adverse drug reactions (11 & 12).

A retrospective DUE is the simplest to perform since drugs therapy is reviewed after patient has received the medication. A retrospective review may detect patterns in prescribing, dispensing or administering drugs to prevent recurrence of inappropriate use and serves as a means for developing prospective standards & target interventions. In retrospective DUE, patients' medical charts or computerized records are screened to determine whether the drug therapy met approved criteria & aid prescribers in improving care for their patients, individually and within group of patients (13). Treatment with AED is a major one generally committing the patient to medication at 1-5 years. AED treatment makes the patient free of seizures. Over all about 70% of children and 60% of adults who have their seizures completely controlled with AED. To withdraw AED patient has to be seizure free for 3 to 4 years since sudden withdrawal increase seizure frequency and severity (14).

**Statement of the problem**

Around 90% of the people with epilepsy in developing countries are not receiving appropriate treatment due to cultural attitude, lack of prioritization, poor health system infrastructure & inadequate supply of AEDs (15). Economic factors are important determinants of clinical decision making & the degree of effect depends on the country & health systems. In developing countries these may be more related to patients' ability to pay & that of availability of drugs (16).

Since epilepsy including: partial, myoclonic–astatic & generalized seizures are in fear of drug resistant, they need to be evaluated both retrospectively and prospectively. Drug use evaluation (DUE) is systematic approach designed to maintain rational use of drugs. DUE can identify problems in drug use, reduce adverse reaction, optimize drug therapy & minimize pharmaceutical related expenditure (17).

The pharmacokinetics of the most frequently prescribed AEDs are complex, which makes dosing and monitoring difficult in any age group; however, treatment decisions become more complicated with the older patient (11). Age related alterations in physiology can affect AED pharmacology & limit the choice of medications. There is a lack of safety & efficacy information to guide clinical decisions about AED

 

therapy in older people. The complexity of medical problems and co-medications among older people requiring AEDs can result in an increased likelihood of drug-related problems & drug interactions, which in turn can affect seizure control and toxicity (18).

Enzyme-inducing drugs such as carbamezepine, oxcarbazepine, Phenytoin, Phenobarbital, primidone & topiramate may accelerate the metabolism of both estrogen & progesterone, thereby reducing their concentration by up to 50%. This increases the risk of pregnancy in patients taking oral contraceptives and suggests the need to increase the dose of steroidal from 35mg to 50mg if an enzyme inducing anti-epileptic drug is given (19). In addition, controlling seizure during pregnancy is vital, as seizures are likely to have an adverse effect on developing fetus. The most common and worrying adverse effects for pregnant women with epilepsy relate to the potential teratogenesis of AEDS. Teratogenic effects are classified as either major malformations or minor anomalies, & both have been associated with maternal AED use (20).

Although seizures are common in the pediatric age group and occurs in approximately 10% of children but current antiepileptic drugs (AEDs) cannot control seizures ill 20-30% of patients. Therefore, new AEDs with greater efficacy & fewer side effects are fiercely needed. (21). Qualified physicians are still prescribing irrational drug combinations, banned drugs and withdrawn drugs. There is a need of mass awareness among physicians & consumers about the concept of essential medicines and use of rational combinations (22).

**Significance of the study**

Medicines have been used irrationally for as long as they have been available. This reduces quality of care, wastes resources and causes harm to the patients. This might be more in developing countries where trained human power, regulation of drug supply & use, drug information, health facility, diagnostic infrastructures, availability of this drugs and health care budget are inadequate. Therefore, anti-epileptic drug use evaluation is a paramount importance in identifying problem area for intervention. Thus, the aim of the present study was to evaluate anti-epileptic drugs with the hospital indicators, so that the data obtained would help and guide to take action. Besides it provides base line information for responsible bodies for monitoring and regulating their drug use pattern.

**Objective of the Study**

**General Objective**

To evaluate use of antiepileptic drugs against pre-set standards in outpatient epilepsy clinic of Bishoftu General Hospital, East Shewa, Ethiopia.

**Specific Objectives**

- To get an insight into the type of seizure
- To describe the drug utilization/prescription pattern of AEDs for the treatment of various forms of epileptic seizure in line with STG
- To evaluate the tolerability of AEDs
- To evaluate the extent of contra indications considered in using AEDs
- To asses drug-drug interaction with co-administered drugs

**METHODS AND MATERIALS**

**Study area and Period**

The study was conducted in Bishoftu General Hospital, Bishoftu town, East Shewa zone, Oromia region, Ethiopia. Bishoftu town is located 47 km far from Addis Ababa. Bishoftu General Hospital has different departments and delivers diversified health care services. The study was conducted from March 10 to May 30, 2014.

**Study design**

A retrospective cross-sectional drug use evaluation was conducted on patient medical records. The necessary data was collected from patient medical cards by using data collection formats and then the result was evaluated against the criteria prepared from the national formulary and standard treatment guide line of Ethiopia for zonal hospitals.

**Population**

**Source population:**

All epileptic patient medical records in the epilepsy Outpatient clinic of Bishoftu General Hospital in the year 2014

**Study population**

All epileptic patient medical records which fulfill inclusion criteria in the epilepsy Outpatient clinic of Bishoftu General Hospital collected from March 10 to April 10, 2014

 

**ELIGIBILITY CRITERIA**

**Inclusion criteria**

All Epileptic patients (irrespective of age, gender and presence of concurrent disease/s) treated in outpatient epileptic clinic of Bishoftu General Hospital in 2014.

**Exclusion criteria**

Patients with other central nervous system disorders like:

- Depression Schizophrenia, Bipolar and Anxiety and
- Unreadable medical card records

**Sampling Technique and Sample Size**

**Sampling Technique**

Systematic random sampling technique was conducted on patients medical records with AEDs prescribed (after every kth, k= 2).

**Sample Size**

The sample size of the study was determined by taking 50% p value, degree of accuracy 5% with confidence interval of 95%, and then the actual size was calculated by using the formula:

$$n=(z^2\ pq)/d^2$$

Where n = the desired sample size

Z = level of significance at 95% confidence interval

P = the proportion in the target population

q = 1- p

d = margin of error

Accordingly; $n=((1.96)^2\ (0.5)(0.5))/(0.05)^2 =384$

Since the number of population (605) is less than 10,000, the sample size was adjusted. Therefore the corrected sample size was:

$$n_f = \frac{n}{1+\frac{n}{N}}$$

Where,

nf = desired sample size

n = sample from infinite population

N = population size, 605 (total number of epileptic patients for one year of 2014)

$$nf = \frac{n}{1+\frac{n}{N}} = \frac{384}{1+\frac{384}{605}} = 235$$

And 10% non-respondents were added to the corrected sample size, and the final sample size was:

(10%*235) + 235 = 259

**STUDY VARIABLES**

**Independent Variables**

Age

Sex

Pregnancy

Diagnosis

Knowledge, attitude & practice of pharmacists

Knowledge, attitude & practice of Prescribers

**Dependent Variable**

Type of seizure (indication)

Dosage regimen (dose, frequency and duration)

Tolerability of AED

Drug interactions

Contraindications

**Data Collection Procedure and Instrument**

**Data Collection Instrument**

Data collection format containing the variables to be assessed was used.

**Data Collection**

After all preliminary preparations for data collections were completed, the data collection format was pre-tested prior to the actual data collection. The data was collected from patients' medical cards by the trained personnel (nurses of the hospital in epilepsy clinic). The collected data was checked for completeness, accuracy and consistency at every step during and after data collection.

**Data Processing and Analysis**

The collected data was cleared, organized and analyzed by using Microsoft excel work sheet. The results were compared with the set criteria, interpreted and presented by using tables.

**Ethical Consideration**

A formal letter was forwarded from Ambo University College of medicine and health sciences, department of pharmacy to Bishoftu General Hospital in order to get permission to conduct the study, and every patient's information was kept confidential.

**Data Quality Assurance**

Training was given to data collectors and the data collection format was pre-tested and consistent supervision of data collection was carried out.

**Operational Definitions**

**Drug use evaluation:** is an ongoing systematic process, designed to evaluate the appropriate and effective use of drugs.

**Adverse drug reaction:** means a noxious and unintended effect of drug that occurs in doses normally used in humans or animals for the diagnosis, prophylaxis or treatment of disease.

**Seizure-free state:** all the seizures stopped.

**Teratogenic:** any substance, agent, or process that induces the formation of developmental abnormalities in a fetus.

**Rational drug use:** rational use of drugs requires that patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements for an adequate period of time, and the lost cost to them and their community.

**Prescription:** any order for drug written and signed by a duly licensed or authorized medical Practitioner used to a patient in order to collect drug from dispensing unit.

**Standard treatment Guideline:** is a guideline designed to be used as a guide to treatment choices and as a reference book to help in overall management of patients.

**Threshold:** is a percentage established by DUE committee, that identifies the point below which a drug therapy problem exists.

**Result**

**Socio-Demographic Characteristics**

A total of 259 patients' medical records were included in the retrospective study. The demographic data revealed that number of males and females patients were 135(52.12%) and 124(47.88%), respectively. The age ranged from 11 months to 67years with 172(66.7%) of patients being independent age group, between 19 and 65 years. 15 (5.83%), 65 (25.1%), 172 (66.7%) and 7 (2.7%) of the patients using AED were in the age group of < 5, 5-18, 19-65, and > 65, respectively. Among females 3(2.4%), 5(4%) and 116(93.5%) that have used AED were pregnant, lactating and neither of the two, respectively. 257 patients were treated because of a seizure and the remaining two patients were because of non-epileptic problems (Table 1).

**Classification of Epileptic Seizures**

Generalized tonic-clonic seizures accounted for almost 48.6%, followed by uncategorized epilepsy (42.5%). Absence seizure (3.90%) and unclassified seizure, idiopathic seizure, and secondary generalized seizure each accounted (1.16%). Thus, the three seizures (secondary generalized seizure, Idiopathic and unclassified seizures) were less common and accounted for 3.48% altogether (Table2).

**Utilization Pattern**

A total of 290 AEDs were prescribed over the study period corresponding to an average of 1.12 AED per patient. In this study 228(78.6%) of patients received prescribed AED in monotherapy and 31(21.4%) with a combination of two drugs. However, polytherapy (> 3 AEDs) was not used. In the group of patients suffering from generalized seizures 120(46.7%) were treated with monotherapy and 22(8.6%) with a combination of two drugs. In the group of patients with partial seizures, all (3) of them were treated with monotherapy (Table 3).

Phenobarbitone was the commonest monotherapy 224 (98.2%) followed by sodium valproate 4 (1.8%). One prescription of each of Phenobarbital and Phenytoin monotherapy is incorrectly indicated for delirium and Pyrogenic meningitis, respectively. Among dual therapies, 18 of them were Phenytoin with phenobarbitone, 10 of them were carbamezepine with phenobarbitone, 2 of them were carbamezepine with Phenytoin and one of them were phenobarbitone with sodium valproate.

**AED Use Profile**

Phenobarbitone (92.8%) was the most frequently prescribed AEDs, followed by Phenytoin (3.8%), carbamezepine (1.7%) and sodium valproate (1.4%). In the group of patients suffering from generalized seizures, phenobarbitone was the most frequently prescribed (92%) followed by Phenytoin (4.14%). Only older AEDs were used when comparing the prescribing pattern of AEDs (Table 4).

**Indications of AEDs**

The majority of patients who were placed on AED were having GTCs with percentage of 49.3%. On the second place AED was majorly presented for un-categorized epilepsy of 44.6%, and thus it was found to be difficult to conclude either as correct or incorrect indication (Table 5).

**The Tolerability of AEDS**

Sixty seven patients were reported because of adverse effects related to his/her anti-epileptic therapy. Headache was the commonest adverse effect faced by 32 patients,

 

**Table 1** Socio-demographic characteristics of patients with the antiepileptic drugs in epilepsy clinic of Bishoftu general hospital from March10 to April 10, 2014

| Socio-demographic variable | | | Number of patients | Percentage |
|---|---|---|---|---|
| **Sex** | Female(F) | | 124 | **47.88%** |
| | Male(M) | | 135 | **52.12%** |
| | Total | | 259 | **100%** |
| **Age group** | <5 | M | 10 | **3.9%** |
| | | F | 5 | **1.93%** |
| | 5-18 | M | 39 | **15.1%** |
| | | F | 26 | **10%** |
| | 19-65 | M | 90 | **35%** |
| | | F | 82 | **31.7%** |
| | >65 | M | 3 | **1.2%** |
| | | F | 4 | **1.5%** |
| | Total | | 259 | **100%** |
| **Female** | Pregnant | | 3 | **2.4%** |
| | Lactating | | 5 | **4%** |
| | Neither of two | | 116 | **93.5%** |
| | **Total** | | **124** | **100%** |

**Table 2** Classification of epileptic seizure in epilepsy clinic of Bishoftu General Hospital from March10 to April 10, 2014.

| S. No | Classification of seizures | No of patients | Percentage |
|---|---|---|---|
| **1** | GTCs(grand mal) | 126 | **48.6%** |
| **2** | Uncategorized epilepsy * | 110 | **42.5%** |
| **3** | Absence seizures (petit mal) | 10 | **3.9%** |
| **4** | SGs | 3 | **1.16%** |
| **5** | GTs | 3 | **1.16%** |
| **6** | Idiopathic seizure | 3 | **1.16%** |
| **7** | Unclassified seizure | 3 | **1.16%** |
| **8** | Myoclonic seizure | 1 | **0.4%** |
| **9** | Atonics seizure | - | **-** |
| **10** | SPs | - | **-** |
| **11** | CPs | - | **-** |
| | **Total** | **259** | **100%** |

* indicates physician diagnosed the disease as "epilepsy" and written the word "Epilepsy" on the patient cards as an assessment rather than classified it.

 

**Table 3** Overall AEDs utilization for the treatment of epileptic seizures in epilepsy clinic of Bishoftu General Hospital from March10 to April 10, 2014.

| S. No. | AED Therapy | Number (percentage) of patients of each AED therapy in each category of epileptic seizure | | | | Total |
|---|---|---|---|---|---|---|
| | | Partial Seizures | Generalized seizure | Unclassified seizure | Uncategorized epilepsy | |
| 1 | **Mono therapy** | 3(1.03%) | 120(46.3%) | 3(1.03%) | 102(35.2%) | 228(78.6%) |
| | Phenobarbitone | 3(1.3%) | 119(46%) | 3(1.3%) | 98(43%) | 224(98.2%) |
| | Sodium valproate | - | 2(0.9%) | - | 2(0.9%) | 4(1.8%) |
| 2 | **Dual therapy** | | 22(15.2%) | | 9(6.2%) | 62(21.4%) |
| | Phenobarbitone + Phenytoin | | 12(19.4%) | | 6(9.7%) | 18(29.1%) |
| | Phenobarbitone + carbamezepine | | 8(13%) | | 2(3.2%) | 10(16.2%) |
| | Phenobarbitone + sodium valproate | | 1(3.2%) | | | 2(3.2%) |
| | Phenytoin + carbamezepine | | 1(3.2%) | | 1(3.2%) | 2(6.45%) |
| 3 | **Polytherapy** | - | - | - | - | - |

Phenobarbitone was the commonest monotherapy 224 (98.2%) followed by sodium valproate 4 (1.8%). One prescription of each of Phenobarbital and Phenytoin monotherapy is incorrectly indicated for delirium and Pyrogenic meningitis, respectively. Among dual therapies, 18 of them were Phenytoin with phenobarbitone, 10 of them were carbamezepine with phenobarbitone, 2 of them were carbamezepine with Phenytoin and one of them were phenobarbitone with sodium valproate.

**Table 4**: AED use profile as a function of the type of epileptics' seizure at Bishoftu General Hospital from March 10 to April 10, 2014.

| Antiepileptic drug | Number of each AED prescribed in each category of epileptic seizure | | | | | Dosage (mg/day) | |
|---|---|---|---|---|---|---|---|
| | Generalized seizures | Partial Seizure | Unclassified Seizure | Uncategorized Epilepsy | Total | Median | **Range** |
| **Phenobarbital** | 133 | 3 | 3 | 133 | 272(92.8%) | 100 | **15 – 300** |
| **Phenytoin** | 6 | - | - | 5 | 11(3.8%) | 100 | **25- 200** |
| **Carbamezepine** | 3 | - | - | 2 | 5(1.7%) | 100 | **100 - 1600** |
| **Diazepam** | 1 | - | - | - | 1(.34%) | 10 | **200 - 1800** |
| **Sodiumvalproate** | 2 | - | - | 2 | 4(1.4%) | 500 | **400 - 2000** |
| **Total** | **145** | **3** | **3** | **142** | **293(100%)** | | |

**Note:** Older (conventional) AEDs: carbamezepine, Phenytoin, phenobarbitone and sodium valproate

 

**Table 5:** Reasons for using AEDs in epilepsy clinic of Bishoftu General Hospital from March10 to April 1, 2014.

| Drug | Reasons for use | Frequency | Percentage |
|---|---|---|---|
| **Phenobarbital** | Grandmal | 119 | 43.8% |
| | GTs | 3 | 1.1% |
| | Absence | 6 | 2.2% |
| | Unclassified epilepsy[a] | 1 | 0.4% |
| | Focal seizure with 2ry generalized | 3 | 1.1% |
| | Idiopathic seizure | 3 | 1.1% |
| | Uncategorized seizure[a] | 114 | 42% |
| | Delirium | 1 | 0.4% |
| **Phenytoin** | Grandmal | 8 | 2.9% |
| | Focal seizure with 2ry generalized | 3 | 1.1% |
| | Pyrogenic meningitis | 1 | 0.4% |
| **Carbamezepine** | Grandmal | 6 | 2.2% |
| | Unclassified Epilepsy[a] | 3 | 1.1% |
| **Sodium valproate** | Grandmal | 1 | 0.4% |
| | Absence | 1 | 0.4% |
| | Uncategorized Seizure | 1 | 0.4% |
| **Total** | | **276** | 100% |

* indicates incorrect use of AED not in accordance with STG.

[a] Unclassified seizures are one of the classifications of seizures including:-Neonatal seizures and infantile spasms.

**Table 6:** The adverse effect faced by the patient at Bishoftu General Hospital from March 10 to April 10; 2014.

| S. No | Adverse effect | Frequency | Percentage |
|---|---|---|---|
| **1** | Headache | 32 | 47.8% |
| **2** | Irritability | 9 | 13.4% |
| **3** | Hypersomnia | 4 | 6% |
| **4** | Confusion | 2 | 3% |
| **5** | Depressed mood | 2 | 3% |
| **6** | Weakness | 3 | 4.5% |
| **7** | Forgetfulness | 4 | 6% |
| **8** | Skin rash | 3 | 4.5% |
| **9** | Nightmare | 2 | 3% |
| **10** | Polyphagia | 1 | 1.5% |
| **11** | Vomit | 3 | 4.5% |
| **12** | Lack of appetite | 2 | 3% |
| | **Total** | **67** | 100% |

Note: - Hypersomnia means sleep lasting for exceptionally long periods.

- Polyphagia means gluttonous excessive eating

 

**Table 7**: Dose and duration of AED used in epilepsy clinic of Bishoftu General Hospital from March 10 to April 10; 2014.

| Indication | Variable | Frequency | Percentage |
|---|---|---|---|
| **Dose** | Correct dose | 230 | **82.4%** |
| | Under dose | 46 | **16.5%** |
| | Over dose | 3 | **1.1%** |
| | Total | 279 | **100%** |
| **Duration** | Correct duration | 261 | **87.3%** |
| | Short duration | 26 | **8.7%** |
| | Long duration | 2 | **0.7%** |
| | No duration | 10 | **3.3%** |
| | **Total** | **299** | **100%** |

All of the above prescriptions were incorrect to mean it didn't fulfill at least one of the following:-Strength, dosage form, route, frequency, duration and the like.

**Table8**: Use of drugs with possible potential interaction with AED but co-administered in epilepsy clinic of Bishoftu General Hospital from March 10 to April 10; 2014.

| Indication | co-administered drug | Frequency | Percentage |
|---|---|---|---|
| **Phenobarbital** | Paracetamol | 7 | **54%** |
| | Oral contraceptives | 3 | **23.1%** |
| **Carbamezepine** | Phenytoin | 2 | **15.4%** |
| **Sodium valproate** | Phenobarbital | 1 | **7.5%** |
| | **Total** | **13** | **100%** |

which was followed by irritability (9 patients) and Hypersomnia (4 patients) (Table 6).82.4% of AED use was containing correct dose. But, 17.6% of AED use was with incorrect dose, of which 16.5% were under dose and 1.1% was over dose regimens. 12.7% of AED therapy contained problem in duration of therapy (Table 7).

**Contraindication**

From the study it was found that no one of AED use was against contraindication.

**Drug-Drug Interaction**

From the total of AED therapy 94.99% was free of any interacting drug and 5.01% of them contained one or more potentially interacting drug (Table 8).

**DISCUSSION**

The demographic data indicated that 52.12% were males and the rest were females. The dominant age group of the study was 19-65 years, followed by 5-18 years.

This indicates the study population was characterized by young and middle age, and that was why the lack of peak in the elderly was seen. Generalized tonic-clonic (48.6%) seizures were the most common type of epileptic seizures encountered. This result is different from a study done on DUE of AEDs at a multispecialty tertiary care teaching Hospital in India (55.22%) (24). Secondly 42.5% of the seizures were left un-categorized. This is most probably due to the professionals are less aware of the type of epilepsy. The key to treating epilepsy is correct diagnosis of the seizure type and, when possible, the type of epilepsy.

Most patients with epilepsy respond to one of the first-line AEDS; second-line agents may be useful in patients who do not respond to one or a combination of the first –line agents. In this study, phenobarbitone (91.7%) was the first-line drug prescribed, followed by Phenytoin (4.14%) and carbamezepine (2.1%) in generalized seizure. The selection

 

of AEDs is increasingly more complex as new agents become available. The best AED therapy is dependent on optimal seizure control and absence of unacceptable side effects (29).

It is important to maintain patients on monotherapy as compliance is better, side effects are less and there is no problem of drug-to -drugs interaction. In this study, 78.6% was monotherapy and only 12.1% was dual therapy. Similarly, a study done in Singapore showed that majority of the patients were on monotherapy (63%) (30). When our result was compared with the above study, there is a wide gap, and this indicates that there is a better use of drug in Bishoftu General Hospital than in Singapore. Phenobarbitone 224(98.2%) was the most frequently prescribed monotherapy, followed by Phenytoin 4(1.8%). In contrast, carbamezepine was the commonest AED used in monotherapy (52%), followed by valproate and phenobarbitone in Singapore (30). Phenytoin with phenobarbitone was the most frequent 2-drug combination in this study. One prescription of each of Phenobarbital and Phenytoin monotherapy is incorrectly indicated for delirium and Pyrogenic meningitis, respectively. This may bring other complication to the treatment receivers and lengths the actual disease diagnosed. Polytherapy offers no advantage over monotherapy. It increases the potential for drug-drug interactions, results in failure to evaluate the individual drugs, can increase the risk of chronic toxicity (including neurocognitive problems), may affect compliance and is associated with a higher cost of medication and necessity for TDM (24).

This study also showed that all epileptics were managed with the conventional AEDs. Phenobarbitone (92.8%) was the most frequently prescribed AEDs, followed by Phenytoin (3.8%) and carbamezepine and sodium valproate which account for (1.7%) and (1.4%), respectively. This may be due the non-availability of newer AEDs within country. Regardless of the blood level, by increasing the dosage form of the same AED gradually to maximum tolerated dose, seizures could be controlled in many patients. Every patient has his/her own necessary dose. For example, the dose of phenobarbitone ranged from 15mg to 300 mg even though most patients needed 100mg per day (Table 5).

In addition, this study has attempted to evaluate the rational use of AEDs among patients treated in epilepsy clinic of Bishoftu General Hospital. The rational use of drugs requires that patient receive medications appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost to them (31). Prescribers must adhere to the STG while prescribing drugs to patients so as to ensure treatment uniformity and promote rational drug use. The study revealed that 8(2.9%) of the indications of AEDs were inappropriate while 150(54.40%) were correctly indicated according to Ethiopia STG. 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. Here, in this study result shows that 75.26% of indications were in line with STG or correct indication. When this result is compared with the threshold set (95%) there is no good prescribing practice towards the stated disease state.

As the adverse effects data were retrieved from patient medical records, it is very likely that adverse effect reporting was under estimated. Most accurate data could have been obtained by questioning the patient directly. Headache (47.8%) was the commonest adverse effect faced, followed by irritability (13.4%) and Hypersomnia (6%). There was correct dosing in 82.4% of AEDs use as per the criteria set for this study. 17.6% of the prescriptions were inappropriately dosed, of which 16.5% and 1.1% were under and over dosed regimens, respectively. The study expressed that 82.4% of the prescriptions of AED were correct dose. This was less than the set criteria (95%). This indicates that there is no better use of drug. In addition, the study indicated there was a problem in duration of therapy in 12.7% of the prescription of which 3.3%, 8.7% & 0.7% were no duration, short duration and long duration, respectively. The study done in Bahrain in May 2008 revealed that low dosing frequency (2.6%) and excessive dosing frequency (0.8%) were noted (27). From the study findings it is evident that the result of correct duration (87.3%) was more or less closer to the set criteria (90%).

In prescribing drugs the prescribers should strictly avoid contra indications, unless the benefit to the patients from using the medication out ways the risks. This study has shown

 

that none of indications of AEDs were against contra indications. So, the result is the same as the threshold of the study (100%).

One purpose of drug use evaluation is to identify those drugs regimens which could result in clinically significant drug-drug interactions. Drug interactions are some of the commonest causes of adverse effects. When two or more drugs are administered to patients they may act independently of each other, or interactions may increase or decrease the effects of the drugs concerned and may cause unexpected toxicity. It is important to remember that interactions which modify the effects of a drug may involve non prescription drugs, non–medical agents, social drugs and certain types of foods. 5.01% of AED therapy, as per this study, had one or more potentially interacting drugs. 94.98% of AED use was free of any interacting drugs. Drug interaction results are more or less similar to the threshold (95%) for AED medications.

Drugs to have correct action at correct size in desirable amount on a time; it should be prescribed in a right dose & frequency. However, this study indicated that the physician or other health professionals did not adhere to this information; as a result wrong dose, frequency error, and drug-drug interaction were observed.

**CONCLUSION**

The finding of this study showed Generalized seizures were the most prominent seizure encountered. Monotherapy was most frequently used in all types of epileptic seizures. The selection of the AEDs corresponds almost well with the known efficacy profile for specific epileptic seizures. Most of the indications are almost appropriate as per the set criteria of the study. Headache was the commonest adverse affect faced by the patients. The most commonly prescribed AED was phenobarbitone, followed by Phenytoin for epilepsy. Most epileptics were managed with the conventional oral AEDs. There was inappropriate usage of AEDs which comprises drug interaction, inappropriate duration of treatment and incorrect dosage regimen. Furthermore, there is poor classification of epilepsy and poor drug history taking by the prescribers. Hence, it is important for health professionals to practice good medical and drug history taking and keeping, as well as good classification of disease state.

In general, the present study has revealed better use of AEDs pertaining to indications and contraindications. However, the classification of seizure as well as the use of drugs with potential drug interactions, dose and duration problem need urgent interventions.

**Recommendation**

☐ Regardless of considerable improvements in health care facilities, rational drug use is still in its early stage in Ethiopia, so the government, ministry of health has to advise method of promoting and implementing rational utilization of drugs.

☐ The prescribers should adhere more to the guide line concerning indications, contra- indications and drug interactions.

☐ The duration of therapy should be according to the STG to prevent under use and over use of AEDs.

☐ Health facilities should undertake Retrospective and prospective drug use evaluations, availability and accessibility of drugs and factors affecting choice of drug treatments problems need to get corrective measures.

☐ Pharmaceutical industries should produce different formulations in needed amount for ease of use.

☐ Drug information centers are appropriate bodies to give any information related to drugs and be established in each health facilities to answer drug related questions of prescribers and customers.

☐ The government, pharmacy schools, ministry of health and pharmacists as a whole must work towards clinical pharmacy adoption which can dramatically reduce drug and therapeutic problems and health care costs.

☐ Finally, it is important for health professionals to practice good medical and drug history taking and keeping, as well as good classification of disease state.

**Abbreviations and acronyms**

| | |
|---|---|
| ADR | Adverse Drug Reaction |
| AEDs | Antiepileptic drugs |
| BGH | Bishoftu General Hospital |
| CPs | Complex partial seizure |
| DUE | Drug use Evaluation |
| GCs | Generalized-clonic seizure. |
| GTCs | Generalized tonic-clonic seizure |
| GTs | Generalized-tonic seizure |
| ILAE | International League against Epilepsy. |

| | |
|---|---|
| JCAHO | Joint commission on the Accreditation of Health care organization. |
| NDP | National Drug Policy |
| PMHRs | Patient Medical Health Records |
| RDUR | Retrospective Drug Utilization Review |
| SGs | Secondary Generalized seizure |
| SPs | Simple partial seizure |
| STG | Standard Treatment Guideline |
| TDM | Therapeutic Drug Monitoring |
| UK | United Kingdom |
| USA | United state of America |
| WHO | World Health Organization |

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