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Original Research Article

A drug utilization study of antiepileptic drugs uses in a tertiary care teaching hospital of India

Soumitra Mandal[1]*, Aruna Donepudi[1], Jabeen Shaik Afshan[2], Suryaprabha Turaga[2]

[1]Department of Clinical Pharmacology and Therapeutics, [2]Department of Neurology, Nizam's Institute of Medical Science, Hyderabad, Telangana, India

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***Correspondence:**
Dr. Soumitra Mandal,
Email: Soumitra.habul@gmail.com

ABSTRACT

Background: Epilepsy is a disorder characterized by repeated seizures due to the disorder of the neurons. Epilepsy needs life-long medical therapy. It is managed by polytherapy. Drug utilization studies help to determine rational combinations of drug use in epilepsy. Aims and objectives of the study were to analyses the drug utilization pattern of anti-epileptics and common types of epileptic seizures and to determine the safety of antiepileptic drugs (AEDs).
Methods: It was a prospective, cross-sectional, observational study. Patients attending neurology epilepsy OPD with h/o seizures and taking at least one antiepileptic were recruited. Data was collected by taking demographic details including brief history of disease, clinical examination and reviewing OPD prescription. Details were recorded in case record form.
Results: We recruited 102 participants (57 male and 45 females) of mean age 29.68±10.52. Mean age of onset of epilepsy was 18.9±10.5 years. Among them 77 (75.4%) were diagnosed as generalized tonic clonic seizures and 18 (17.6%) were diagnosed as focal seizures. Monotherapy was given in 31 (30.3%) patients while polytherapy was given in 71 (69.7%) patients. Valproic acid was most commonly used monotherapy (12 patients). No fixed drug combinations were used. Clobazam in 55 (53.9%) patients and valproic acid in 53 (51.9%) patients were prescribed. The other AEDs prescribed were lamotrigine, oxcarbazepine, carbamazepine, lacosamide, zincosamide, perampanel, and phenytoin. All antiepileptics were prescribed in brand name. The prescribed daily dose (PDD) was less than defined daily dose (DDD) as per anatomical therapeutic chemical (ATC) classification. Two adverse effects were reported during study period. They were mood change and blurring of vision in two different patients.
Conclusions: The PDD was less than DDD as per ATC classification. Awareness should be created among neurologists to prescribe more generic drugs because of their cost effectiveness. Studies are needed with larger sample size to analyze the drug utilization patterns which helps in the planning of reduction of expenditure for the patient without compromising efficacy.

Keywords: Epilepsy, Drug utilization, Antiepileptics

INTRODUCTION

Drug utilization research was defined by WHO 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. The study of drug utilization is an evolving field. The importance of drug utilization studies has been increasing due to heightened marketing of new drugs, widespread variations in the prescribing pattern of drugs and its consumption, increasing concerns about late onset adverse effects and the concern with respect to drug costs.[1] Epilepsy is a disease of the brain defined by any of the following conditions:[2] 1) At least two unprovoked (or reflex) seizures

occurring >24 hours apart, 2) One unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next 10 years 3. Diagnosis of an epilepsy syndrome.

Epilepsy is a common, chronic neurological disease which requires long term treatment and poses a heavy burden on health-care system. Pharmacotherapy of epilepsy only provides symptomatic relief. The AEDs were also used for various other conditions like prophylaxis of manic disorder and neuropathic pain.[3]

It is recommended that the epidemiologic study of epilepsy should follow the guidelines formed by the international league against epilepsy (ILAE) commission of epidemiology and prognosis.[4] The type of epilepsy determines the most appropriate choice of drug therapy for a patient with seizure. Single drug therapy is the usual treatment recommended initially as:

It has fewer drug interactions and side effects, cost effective, better tolerability, better medication compliance, and good quality of life. Polytherapy is needed only for patients with multiple seizure types or refractory diseases. Major expenditure related to the treatment lies with the purchase of second-generation AEDs, which are more expensive compared to the first-generation agents. Drugs such as gabapentin, lamotrigine, vigabatrin, topiramate, tiagabine, and zonisamide are the newer ones and currently used as add-on or alternative therapy. They have lesser adverse effects.[5-7]

In this context, and considering that there are few studies on antiepileptic use in southern India, we aimed to determine the utilization pattern of these drugs in a tertiary hospital. Hence this study was planned to assess the number of AEDs used per prescription, and the prescriptions are as per standard guidelines or not.

METHODS

The present study was a prospective, cross sectional, observational study. It was conducted in the department of clinical pharmacology and therapeutics and department of neurology, NIMS, after NIEC approval. (45th ESGS no. 936/2019). Study duration was of 3 months (December 2019 to march 2020). Inclusion criteria were patients having history of seizures, aged between 18 to 65 years of either gender and prescribed at least one epileptic drug. Exclusion criteria were seizures associated with acute causes like paralytic stroke, trauma and patients having status epilepticus.

Written informed consent was taken from all the study participants prior to enrolment into the study. All the OPD prescriptions were screened. Data was collected by taking brief medical and treatment history, clinical examination. Type of epilepsy, AEDs prescribed, dose, duration, any fixed dose combinations (FDCs), generic and branded drugs of all AEDs were recorded in case record form. Study outcomes were common types of epilepsy, average age of on-set of seizures, Number of antiepileptics prescribed per patient, most commonly prescribed AEDs, to compare PDD with DDD.

Statistical analysis

Data was presented as mean ± SD for continuous variables, proportions for nominal variables. Statistical analysis was performed using Microsoft excel software for data stratification and analysis.

RESULTS

One hundred and two patients were enrolled into the study. Enrolment of patients was stopped due to sudden outbreak of COVID-19 pandemic. Mean age of the participants was 29.68±10.52 years. Demographic characteristics were shown in Table 1.

Table 1: Demographic characteristics, (n=102).

Patients' characteristics	Mean ± SD
Age (years)	29.68±10.52
Gender (%)	
Male	57 (55.88)
Female	45 (44.11)
BMI (kg/m^2)	23.09±3.07
Average number of antiepileptics per prescription	2.4
Average no. antiepileptics as generics	Nil
Number of FDC	Nil

The average age of on-set of seizures in participants was 18.9±10.5 year. The most common types of seizures observed were generalized tonic clonic seizures (75.49%) and focal seizures (17.64%). Various types of epilepsies observed were denoted in Table 2.

Table 2: Types of seizures observed, (n=102).

Types of seizures	Observed (%)
Generalized tonic clonic seizures	77 (75.49)
Focal seizures	18 (17.64)
Myoclonic seizures	2 (1.96)
Absence seizures	2 (1.96)
Clonic seizures	1 (0.98)
Secondary generalized seizure	1 (0.98)
Non classified	1 (0.98)

More than 3 drugs were prescribed for most of patients (49.01%). Mono-therapy constituted 30.39% and Dual drug therapy 20.58%. Actual number of antiepileptics prescribed per patient were depicted in Figure 1.

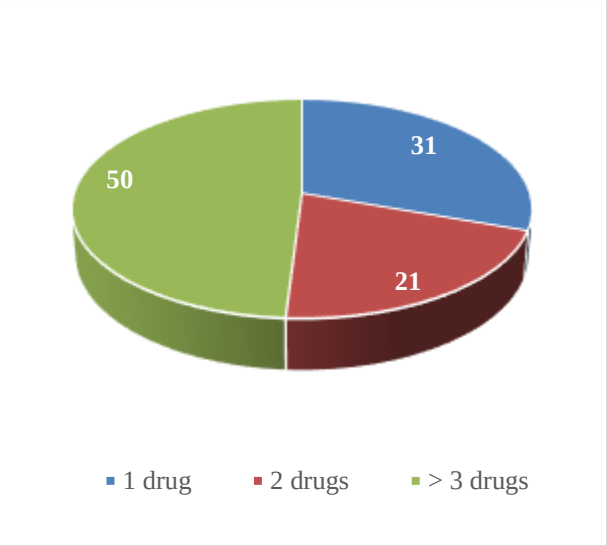

Figure 1: Number of antiepileptics prescribed per patient.

The number of patients prescribed monotherapy were 31 out of 102. Among the patients prescribed monotherapy, Valproic acid was the most commonly prescribed drug (12 patients) followed by oxcarbazepine 7, levetiracetam 7, phenytoin 4, lamotrigine 1 (Figure 2).

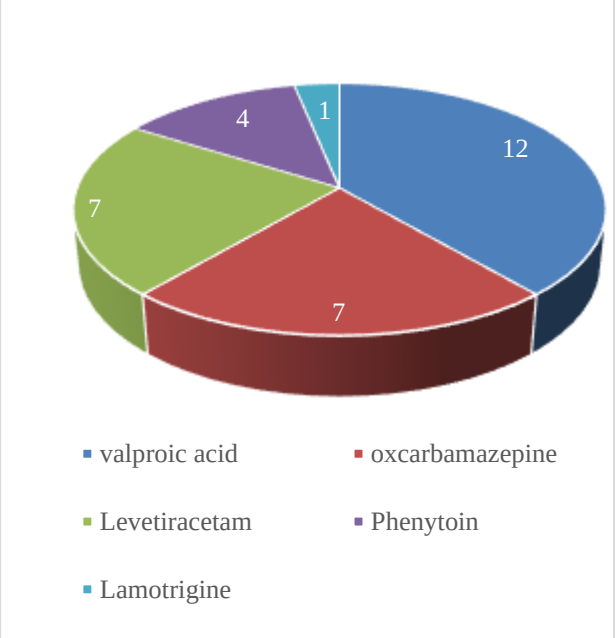

Figure 2: Antiepileptic monotherapy.

None of the patients were prescribed generic drugs and FDCs. The doses of AEDs prescribed in this study were less than that of DDD of each drug except for brivaracetam and phenobarbital (Table 3).

Two adverse effects were reported during the study period. They were mood changes due to levetiracetam and blurring of vision in phenytoin therapy patients.

Table 3: Antiepileptics utilization pattern.

Drugs	Nomenclature	DDD as per ATC[8] (gm)	PDD (gm)
Lamotrigine	N03AX09	0.3	0.153
Clobazam	N05BA09	20 mg	9.37 mg
Perampane	N03AX22	8 mg	3.56 mg
Valproic acid	N03AG01	1.5	0.471
Zonisamide	N03AX15	0.2	0.192
Carbamazepine	N03AF01	1	0.513
Phenytoin	N03AB02	0.3	0.287
Oxcarbazepine	N03AF02	1	0.817
Lacosamide	N03AX18	0.3	0.174
Levetiracetam	N03AX14	1.5	0.887
Brivaracetam	N03AX23	0.1	0.166
Phenobarbital	N03AA02	0.1	0.15

DISCUSSION

In the present study average age of onset of seizures was found to be 18.9±10.5 years, which was similar from finding of other such study.[5] In our study, the epilepsy is most prevalent in males compared to females, which is consistent with studies conducted by Arulkumarana et al and Patel et al.[9,10] Most common type of seizure noted was GTCS, which is consistent with the findings of other studies. Average number of anti-epileptics per prescription was 2.42 in our study, which is higher when compared to study by Arunkumaran et al.[9]

It was found in our study that none of the AEDs prescribed by generic names, in spite of the fact that generic drugs are cost effective when compared to brand ones. The results of our study highlight significant unawareness of the process of generic substitution among both patients and neurologists and reveal a general level of discomfort among neurologists to prescribe generic AEDs. Our results were consistent with one survey.[11] For those anti-epileptics with narrow therapeutic index, the value of sticking to the brand name is also crucial because switching from one brand to a generic drug might not be therapeutically comparable to the branded drug, which may put patients at risk of breakthrough seizures or other adverse events.[12,13]

We found that valproic acid was the most commonly prescribed broad spectrum antiepileptic drug. Valproic acid was found to be the most commonly used drug in other studies also. Some studies reported phenytoin as one of the most commonly used drugs due to its low cost and fair seizure control rate which allows its large-scale use.[6,7] In contrast, our study reported lower use of phenytoin due to its pharmacokinetics and side effect profile.

We have found that 30.39% patients were prescribed monotherapy of antiepileptic drug. Our finding is in

contrast to a study conducted by Patel et al which reported 70.6% patients were prescribed monotherapy.[10] The difference may be due to the inclusion of patients who were prescribed anti-epileptic drugs for non-epileptic conditions. In another study monotherapy was given in 57.89% of patients. But the sample size was less (n=38) in this study.[12] It was also found that 49.01% of patients were prescribed >3 drugs, which is higher when compared to other studies. The literature says that chances of drug-drug interactions were increased with polytherapy. The reason for higher percentage of our patients on polytherapy, is due to higher number of drug resistant epilepsies who were referred from other centres for further management.

DDD greater than PDD was found in all AEDs except brivaracetam and phenobarbital probably to avoid the side effects. Newer ones perampanel, topiramate and lamotrigine were used to a very less extent. This may be due to the fact that newer antiepileptics are costly as compared to conventional ones. Several factors affect the selection and acceptance of anti-epileptic drugs by doctors, including the age, patient gender, weighting of effectiveness against possible ADRs, epilepsy syndromes and type, comorbid conditions, peer advice, familiarity with treatment of AEDs, and healthcare system prevailing in a specific area. Drug utilization studies help to assess prevailing health care practices, so that lacunae in the system can be found out and strategies can be planned to rectify them.

Limitations

The limitations of this study were smaller sample size and shorter study period.

CONCLUSION

The PDD was less than DDD as per ATC classification. Awareness should be created among neurologists to prescribe more generic drugs because of their cost effectiveness. Further studies with larger sample size are needed to help the physicians to administer cost effective drugs to the patient and to initiate strategies for reducing the irrational prescribing of AEDs and help the government to frame policies for medical reimbursement programs.

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