JAMP

A CROSS SECTIONAL STUDY ON PATTERNS OF ANTI EPILEPTIC DRUG USAGE IN TERTIARY CARE PUBLIC SECTOR HOSPITAL

Anu M[1], Poornima B[2], Basavanna P L[3], Ananthakumar P K[4]

[1]Assistant Professor, Department of Pharmacology, Vels Medical College and Hospital, Tiruvallur, Tamil Nadu, India.
[2]Assistant Professor, Department of Pharmacology, Akash Institute of Medical Sciences, Bangalore, India.
[3]Professor, Department of Clinical Pharmacology, Mysore Medical College & Research Institute, Mysore, India.
[4]Associate Professor, Department of Medicine, Saveetha Medical College and Hospital, Chennai,Tamil Nadu India.

Abstract

Background: Epilepsy is a chronic disorder characterized by recurrent unprovoked seizures. The aim of treatment is complete control of seizures without any untoward reaction due to medications. Drug utilisation reviews help to review and assess the appropriateness of the prescription drug use and prescribing patterns. **Aim & Objectives:** To study the prescription patterns of Antiepileptic drugs (AEDs) among epileptic patients attending outpatient departments of a tertiary care hospital. **Materials and Methods:** A cross-sectional observational study, spanning one year three months was conducted in the OPDs of Neurology, Medicine, Psychiatry and paediatric departments. Study included patients with epilepsy, who were on antiepileptic drugs, on follow up for minimum one year, all age groups and both sexes. WHO indicators were used for analysing the prescriptions. **Results:** 207 prescriptions were studied. 57.5% were males, generalised seizures were the most common type and mono therapy was preferred in majority of the subjects. Average number of AEDs prescribed were 1.53, Phenobarbitone was the most preferred AED. **Conclusion:** Older AEDs are still preferred. Mono therapy improves the treatment outcomes by reducing drug interactions and adverse events.

INTRODUCTION

Epilepsy is a one of the most common neurological disorders and the second most common chronic neurological condition seen by neurologists.[1] It is neurological disorder that results from recurrent, unprovoked and hypersynchronous discharge of a set of neurons in brain and referred as epileptic seizures.[2] The incidence and prevalence of epilepsy shows substantial geographical heterogeneity.[1] Epilepsy is believed to affect 1% to 2% of the population; approximately 2 million people have been diagnosed with epilepsy. The incidence is highest in childhood and old age.[3] Epidemiological studies of epilepsy from around the world have shown prevalence rates ranging from 0.9 - 57 per 1000 population, with higher prevalence rates for developing countries.[4]

The overall aim in treating epilepsy should be complete control of seizures, without causing any untoward reaction due to the medication. A large number of drugs are currently available for the treatment of epilepsy. Older/conventional drugs are commonly used as first line drugs. They are relatively less expensive than the newer antiepileptics. Newer AEDs or second line agents are currently used as add-on or alternative therapy. They have lesser adverse effects and have few, if any, drug interactions.[5] Monotherapy is usually recommended in epilepsy but polytherapy is often required for patients with multiple seizure types or refractory disease. Polypharmacy is usually associated with higher incidence of adverse effects, drug interactions and added costs.[6]

Drug utilization review (DUR) is a review and assessment of the appropriateness of prescription drug use and also the prescribing patterns. These studies serve as means 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.[2]

Our study was conducted at a tertiary care hospital attached to a teaching institute. This study focuses on the prescription patterns of AEDs in different types of epilepsy using the World Health Organization/International Network of Rational Use of Drugs (WHO/INRUD) prescribing indicators.

MATERIALS AND METHODS

After obtaining the institutional ethical committee clearance we conducted a cross-sectional observational study in the outpatient departments of Neurology, Medicine, Pediatrics and Psychiatry departments. The study was conducted over a period of one year three months. The sample size was calculated using 5% as the prevalence of epilepsy, at 5% significance and 20% error and found to be 207. As per the inclusion criteria patients with epilepsy, who were on antiepileptic drugs, on follow up for minimum one year, all age groups and both sexes were included in the study. Subjects with comorbid conditions like psychotic disorder, mental retardation, dementia in elderly, depression, those with acute symptomatic seizure secondary to Strokes, head injuries, neuro infection, metabolic causes such as Hepatic Failure, Renal Failure, Cardiac failure, etc., Brain tumors, subjects who have had recent brain surgery were all excluded from the study. After obtaining written informed consent the required demographic data like the age, gender, educational status, occupation, monthly family income and socioeconomic status were collected in a preformed proforma.

The data was analyzed using Statistical Package for Social Sciences (SPSS) 20 version. Descriptive statistics and inferential statistical tests like the Crosstabs and t – test for independent variables were used.
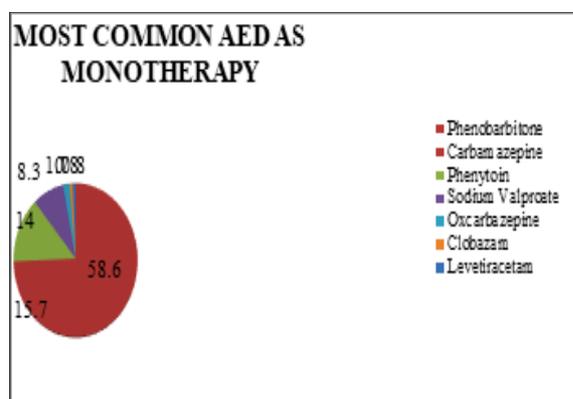
RESULTS

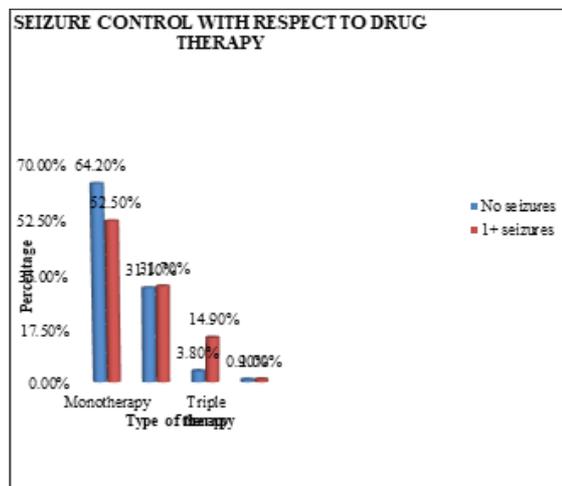**Figure 1: Most Common AED as Monotherapy**

Figure 2: Seizure Control with Respect to Drug Therapy

A total of 207 patients who fulfilled the inclusion criteria were observed for the AED therapy. The demographic details have been shown in table 1. Of these the 57.5% were males and 42.5% were females. The male to female ratio was 1.35:1. The age range of the study population was 2 - 80 yrs with majority of the subjects belonging to the age group 11 – 40 yrs (68.1%). We observed that 30.4% of the subjects had an educational qualification up to high school and 23.2% were illiterate.

Using updated BG Prasad SES classification, January 2014 we found a majority of study subjects belonging to the lower middle socioeconomic class (34.8%) followed by lower class of SES (26.7%) and only 4.8% belonged to upper class. Subjects were grouped using the International League against Epilepsy (ILAE) Commission on Classification and Terminology, 2010, and seizures were broadly classified as Generalised, Focal and unclear types based on the records available with the subjects. In the present study Generalised seizures (50.7%) were the most common type of seizures seen followed by focal seizures (30%) and unknown type were seen in 19.3% of the subjects.

AED monotherapy was given to 58.5% of the subjects, dual therapy to 32.9%, triple drug to 7.7% and 1% received quadrple drug combination. There were 13 types of two drug combinations, 8 types of three drug combinations and two types of four drug combination. Most common two drug combination was Phenobarbitone + Phenytoin and most of the three drug combination was Phenobarbitone + Phenytoin + Carbamazepine. The most commonly prescribed drug as monotherapy was Phenobarbitone followed by Carbamazepine and Phenytoin. Among the newer antiepileptics prescribed as monotherapy the most common was Oxcarbazepine followed by Clobazam and Levetiracetam. 51.2% of the subjects had good seizure control in the previous six months, 64.2% of whom were on monotherapy. Using the WHO/INRUD (World Health Organization/International Network of Rational Use of Drugs) prescribing indicators we found the

215

average number of antiepileptic drugs per prescription was 1.53. Percentage of drugs prescribed using generic names was 80.44%. Out of all the prescribed AEDs 77.2% drugs were by available from hospital pharmacy. All the antiepileptic drugs enlisted in the National list of essential medicines 2011 were available in our hospital pharmacy.

We also had 47 subjects whose medications were changed, or dose adjusted. The reasons were adverse effects, breakthrough seizures, economic reasons and drug default. Ten subjects had reported adverse effects as the cause for change in medications.

Table 1: Demographic Details

GENDER	
Male	**57.5**
Female	**42.5**
AGE	PERCENTAGE
0 - 10	4.3
11 - 20	18.4
21- 30	25.1
31 - 40	24.6
41 - 50	12.1
51 - 60	10.6
>60	4.8
OCCUPATION	PERCENTAGE
Unskilled labour	30
Skilled labour	20.8
Student	18.8
Unemployed	17.4
Home maker	13.0
EDUCATIONAL STATUS	PERCENT
Illiterate	23.2
Primary	15.5
Middle	14.5
High School	30.4
Higher Secondary	7.7
Graduate/ PG	8.7
SOCIO-ECONOMIC STATUS	PERCENTAGE
Lower class	26.1
Lower middle class	34.8
Middle class	21.7
Upper middle class	12.6
Upper class	4.8

Table 2: Who/INRUD Prescribing Indicators

PRESCRIBING INDICATORS	OBTAINED VALUES
Average number of drugs per encounter	1.53±0.72
Percentage of drugs prescribed by generic name	80.44%
Drugs prescribed from hospital pharmacy	77.2%

Table 3: Seizure Frequency in Six Months

NUMBER OF SEIZURES IN LAST 6 MONTHS	PERCENT
0	51.2
1 or more	48.8

DISCUSSION

Our study highlights a male preponderance in epilepsy with a male female ratio of 1.35:1. Similar observations were made in other studies like S.Palanisamy et al,[7] Joseph et al,[8] and Sachchidanand Pathak et al.[9] But Kariyawasm SH et al,[4] differed by reporting a 1:1 male:female ratio. While the reasons behind gender differences are not clear, it has been generally observed that men have a higher incidence of focal epilepsy while women are influenced by genetic factors or hormones leading to a higher incidence of generalized epilepsy.[6] Most of the study subjects (58.5%) had been prescribed monotherapy. Monotherapy offers many advantages like better compliance, lesser drug – drug interactions and fewer side effects. But in cases that are refractory to monotherapy more than one drug is unavoidable. There is no evidence from randomized controlled studies that shows polytherapy is superior to monotherapy in achieving seizure control.[6] Generalised seizures (50.7%) were the most common type of seizures seen followed by focal seizures (30%) and unclassified type were seen in 19.3% of the subjects. The majority of hospital-based studies have recorded a higher frequency for partial epilepsies, while the community based studies recorded a higher frequency for generalized seizures. The overlooking of most striking symptom by the respondents and interviewer for the generalized seizures and misclassification of partial seizures with secondary generalization as generalized seizures in

216

community studies could be the possible reason for observed differences between hospital and community based studies.[10]

Most prescribed Antiepileptic drug in monotherapy was Phenobarbitone (58.6%) followed by carbamazepine (15.7%). and phenytoin (14%). This trend was similar to one study from India,[11] and a study done in Ethiopia.[12] Phenobarbitone is one of the oldest AED available. Many other studies preferred other drugs like phenytoin and carbamazepine like Badwaik RT et al,[13] Vettikkadan et al,[14] and Kariyawasam SH et al.[4] Though phenobarbitone is not the preffered first line agent according to guidelines,[15] it may be used frequently due to the low cost of the drug, good seizure control, all round availability of the drug and also because most of the subjects were on long term follow ups (average follow up years of the subjects was 10.3 years).

In our study Good control (no seizures in the past six months prior to the interview) was seen in 51.2% and poor control (having one or more episodes of seizures in the past six months) in 48.8% of subjects. Other studies like Kariyawasam SH et al,[4] and a study conducted by Sebastian J (16) had similar seizure control like 59.66% and 59.7% respectively. Epilepsy can be treated effectively in approximately 60% of patients who become seizure free with the first or second line antiepileptic drug (AED) that they are prescribed.[9]

We used the WHO/INRUD prescribing indicators to study the rationality of the prescriptions. Most of the prescribing indicators were near optimum. Anirudha Potey et al. had similar results but the drugs prescribed from hospital formulary and generic prescribing was low compared to our study.[17]

The most common combinations used among the two drug combination in our study are the Phenobarbitone + Phenytoin (41.2%) and among the three drug combination phenobarbitone + phenytoin + carbamazepine was the most common at (43.8%). This finding was similar to Badwaik et al,[13] a study done by Sebastian J,[16] and a study done in Amritsar by Deepalakshmi M,[3] found similar combination in dual drug therapy but differed in triple drug therapy with Phenytoin + Phenobarbitone + levetiracetam being commonly used.

Combining two antiepileptic medications needs to follow certain criterias like both the drugs should have a different mechanism, should not have complex pharmacokinetic interactions, should not have a similar adverse effect profile and can be combined in minimum doses to produce maximum effect.[18]

CONCLUSION

In our study generalized seizures were most prominent followed by partial seizures. Most of patients are young and epileptic seizures are more common in men. Monotherapy was most frequently used. The principles of prescription were compliant with the prescription indicators mentioned by WHO/INRUD.

REFERENCES

1. Pal A, Prusty SK, Sahu PK, Swain T. Drug utilization pattern of antiepileptic drugs: a pharmacoepidemiologic and pharmacovigilance study in a tertiary teaching hospital in India; Asian Journal of Pharmaceutical and Clinical Research 2011;4(1):96-99.
2. Mazhar F, Shamim S, Malhi SM. Drug utilization evaluation of antiepileptics in three selected multidisciplinary teaching hospitals of Pakistan; Int J Pharm Pharm Sci 2014;6(5):59-66.
3. Deepalakshmi M, Gupta M, Ahuja S. Observational Study of Prescribing Pattern of Antiepileptic Drugs in Tertiary Care Hospital. IOSR-JPBS 2014;9(1):12-20.
4. Kariyawasam SH, Bandara N, Koralagama A, Senanayake S. Challenging epilepsy with antiepileptic pharmacotherapy in a tertiary teaching hospital in Sri Lanka; Neurol India 2004; 52:233-7.
5. Mathur S, Sen S, Ramesh L, Kumar SM. Utilization pattern of antiepileptic drugs and their adverse effects, in a teaching hospital; Asian Journal of Pharmaceutical and Clinical Research January-March 2010;3(1).
6. Haroon A, Tripathi M, Khanam R, Vohora D. Antiepileptic drugs prescription utilization behavior and direct costs of treatment in a national hospital of India; Ann Indian Acad Neurol 2012;15:289-93.
7. ArulKumaran K.S.G, Palanisamy S, Rajasekaran A; A Study On Drug Use Evaluation Of Anti-Epileptics At A Multispecialty Tertiary Care Teaching Hospital; International Journal of PharmTech Research; Oct-Dec 2009; Vol.1, No.4, pp 1541-1547
8. Joseph N, Kumar GS, Nelliyanil M. Pattern of seizure cases in tertiary care hospitals in Karnataka state of India; Ann Indian Acad Neurol 2013;16:347-51.
9. Pathak S, Singh L, Singh T, Sharma SK. Prescribing patterns of anti-epileptic drug in different age group in India; Journal of Drug Discovery and Therapeutics 2013;1(7):69-75.
10. Amudhan S, Gururaj G, Satishchandra P. Epilepsy in India I: Epidemiology and public health. Ann Indian Acad Neurol. 2015 Jul-Sep; 18(3): 263–277
11. Elizabeth ST, Kia RA, Yagnik RM, Nagaraju K. Prescribing Pattern of Antiepileptic Drugs in Adults in a South Indian Tertiary care Hospital; Indian Journal of Pharmacy Practice Jan - Mar, 2012;5(1).
12. Gurshaw M, Agalu A, Chanie T. Anti-epileptic drug utilization and treatment outcome among epileptic patients on follow-up in a resource poor setting; Journal of Young Pharmacists 2014;6(3):47-52.
13. Badwaik RT, Mahajan HM, Borkar AS, Honrao R, Chopade SS. A Drug Utilization Study of Antiepileptic Drugs Use in a Tertiary Care Hospital of Central India; J Cont Med A Dent 2015;3(2):33-38.
14. Vettikkadan A R, Jith A, Krishnaveni K, Kumar S R; Study of Utilization Pattern And Drug Interactions Of Anti-Epileptic Drugs In A Private Hospital; Asian J Pharm Clin Res, Vol 7, Issue 5, 2014, 164-166
15. Goldenberg MM. Overview of drugs used for epilepsy and seizures etiology, diagnosis, and treatment; P&T July 2010;35(7)
16. Sebastian J, Adepu R, Keshava BS, Harsha S. Assessment of antiepileptic drugs usage in a South Indian tertiary care teaching hospital; Neurology Asia 2013; 18(2):159 – 165.
17. Mane YV, Potey A, Bhide S S, Jalgaonkar SV, Ravat SH; Drug Utilization Pattern of Antiepileptic Drugs and Direct and Indirect Cost Estimation In The Treatment Of Epilepsy At Tertiary Care Hospital; International Journal of Information Research and Review; Vol. 2, Issue, 06, pp. 759-764, June, 2015
18. Mani J. Combination therapy in epilepsy: what, when, how and what not!; supplement to Journal of the association of physicians of India, august 2013;61.