



## **Studies On Drug Use Pattern of Anti-Epileptic Drugs In A Tertiary Care Rural Teaching Hospital**

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### **ABSTRACT**

Many new antiepileptic drugs (AEDs) have become available in recent years. Investigations of prescription patterns and exposure of AEDs to different patient groups are important regarding drug safety aspects. To evaluate the drug use pattern of antiepileptic drugs (AEDs) and other medications in a representative population attending tertiary care rural teaching hospital. Methodology: The prospective observational study was conducted during a period of 6 months at tertiary care hospitals at Palakkad. This study was approved by the Institutional Ethics Committee. Patient data collection forms were prepared based on the study objectives. The data collection forms are filled which included all the demographic and relevant clinical information like Name, age, gender, marital status, epilepsy diagnosis, antiepileptic medications, duration of therapy etc. 30% (n=67) of patients were prescribed with combination of two drug. Sodium valproate and levetiracetam is the most frequently used (n=18, 8.07%) followed by Sodium valproate and clobazam (n=11, 4.93%). In this study two drug combinations have a better production against epileptic patients. In our study concluded that the combination therapy may seem costlier than monotherapy in the short term, but when used appropriately, it causes significant savings: lower treatment failure rate, lower case-fatality ratios, and fewer side-effects than monotherapy, slower development of resistance and consequently, less money needed for the development of new drugs.

**Keywords:** AEDs, Drug use pattern,

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Received 08 July 2017, Accepted 12 July 2017

## INTRODUCTION

Antiepileptic drugs (AEDs) are the mainstay of the therapy for epilepsy, despite the development in recent years of new therapeutic options, such as brain stimulation [1] or surgery [2]. In the last years, several pharmacoepidemiological studies documented a growing trend in AED use, particularly in elderly patients [3, 4] and the elderly have become the population with the highest growth for epilepsy [5, 6]. The prevalence of this disease ranges from 6.01 per 1000 in patients between 65 and 69 years to 7.73 per 1000 in patients aged over 85 years [7] and is about two-fold the prevalence among younger adults with a higher burden in nursing home residents [8, 9]. Moreover, the annual incidence of epileptic disorders rises from 90 per 100 000 in people between 65 and 69 years to more than 150 per 100 000 in people over 80 years [10, 11]. In the last 15 years, several compounds have been newly marketed. For this reason, AEDs are traditionally divided into two classes: older AEDs (marketed before 1991) and newer AEDs (marketed from 1991) [12, 13]. First and foremost, newer AEDs were developed to be used together with older AEDs as add-on therapy in epileptic patients with a suboptimal control of epilepsy. Nevertheless, some of these newer agents such as lamotrigine, levetiracetam, oxcarbazepine and topiramate are also currently approved in Italy as monotherapy for the treatment of epilepsy.

More recently, various AEDs have been approved for indications other than epilepsy, such as mood disorders or neuropathic pain [14] and an increased use of these compounds has been observed in different countries [3, 4] both for labeled and unlabelled indications [15, 16]. With regard to this, valproic acid, carbamazepine and lamotrigine are approved in the treatment of various phases of bipolar disorder, while gabapentin and pregabalin are approved for neuropathic pain.

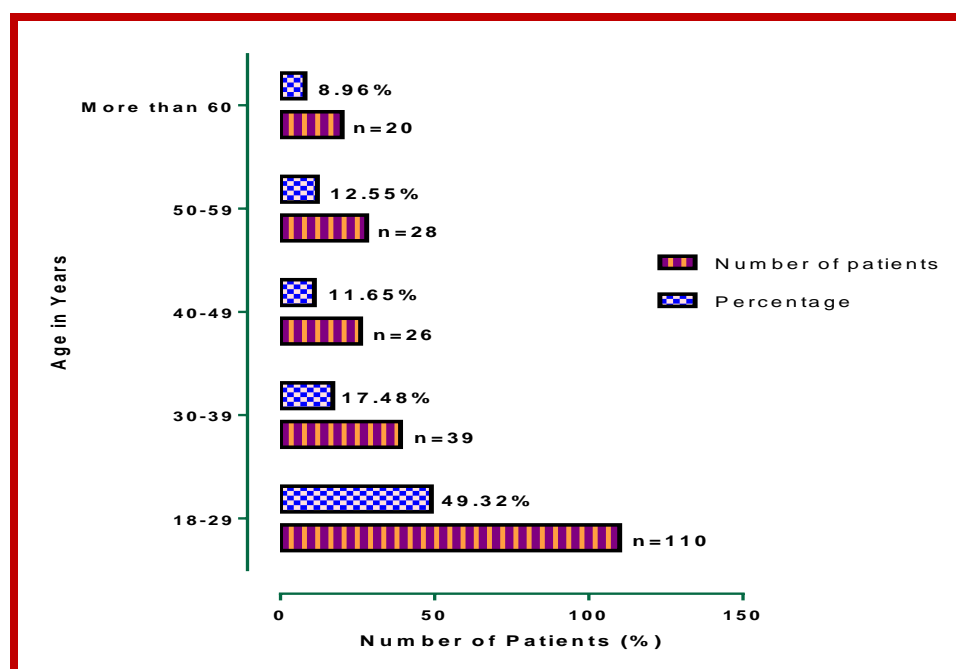
## MATERIALS AND METHOD

The prospective observational study was conducted during a period of 6 months (December 2016- May 2017) at tertiary care hospitals at Palakkad. This study was approved by the Institutional Ethics Committee. Patient data collection forms were prepared based on the study objectives. A total of 223 patients diagnosed with epilepsy fulfilled the inclusion criteria were recruited in the current study. The patients included in the analysis were, Both inpatients and outpatients with Epilepsy with or without co morbidities, patients with age greater than 18 years and patients on both sex. Those who excluded from the analysis were patients below 18 years, pregnant women and patients who are not willing to participate in the study. The data collection

forms are filled which included all the demographic and relevant clinical information like Name, age, gender, marital status, epilepsy diagnosis, antiepileptic medications, duration of therapy etc. The summarized data's was carried out the descriptive analysis by using the software Graph pad Prism version 6.

## RESULTS AND DISCUSSION

Based on the inclusion and exclusion criteria, 223 respondents were enrolled in this study. According to Gender wise distribution demonstrates that out of 223 Epilepsy patients 38.56% (n=86) were males and 61.43% (n=137) were females and it shows that females are more affected than males. Among 223 patients diagnosed with Epilepsy, 49.32% were in the age group 18-29years, 17.48% were in age group 30-39 years, 11.65% were in the age group 40-49 years, 12.55 % were in the age group 50-59 years, and 8.96 % were in age group of  $\geq 60$  years. The majority of the patients were in the age group between 18-29 years.



**Figure 1: Age wise distribution**

The distribution of marital status of the epilepsy patients was denoted in Table 3. Out of the 223 patients, the majority of the patients, i.e., 56% (n=125) patients were unmarried and remaining 44% (n=98) were married. Among 223 patients 31.39 % (n=70) were employed 52.46% (n=117) were unemployed, 14.34% (n=32) were students and 1.79% (n=4) were retired and the results showed that most of the epilepsy patients were unemployed.

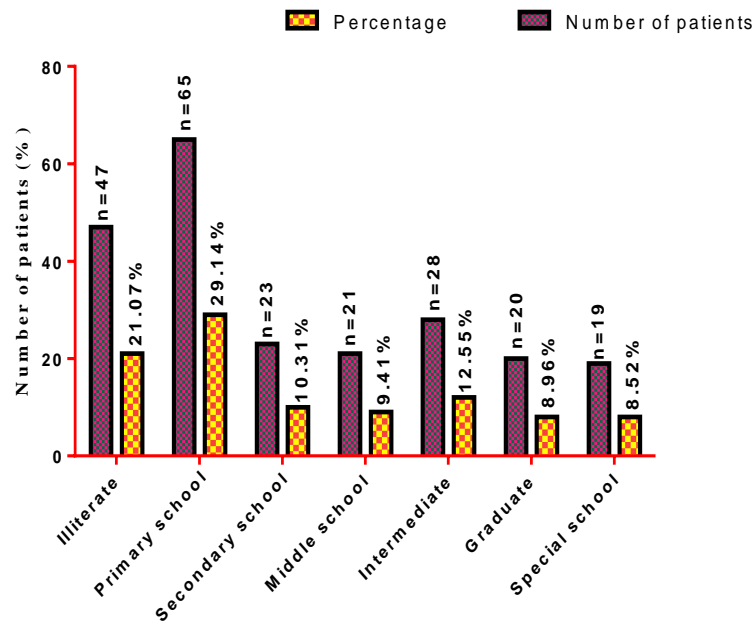


Fig no 2 : Educational Status

### Figure 2: Educational status

According to the educational status out of 223 patients 18.38% (n=41) were illiterate, 20.62% (n=46) were attended primary school, 3.58% (n=8) were studied at secondary school, 8.07% (n=18) were attended middle school, 11.65% (n=26) were obtained intermediate education, 8.96% (n=20) patients were graduating, 7.17% (n= 16) were facing learning difficulty, 6.72% (n=15) attended special school and 14.79 % (n=33) were left school due to epilepsy. The majority of the study subjects were attended primary school.

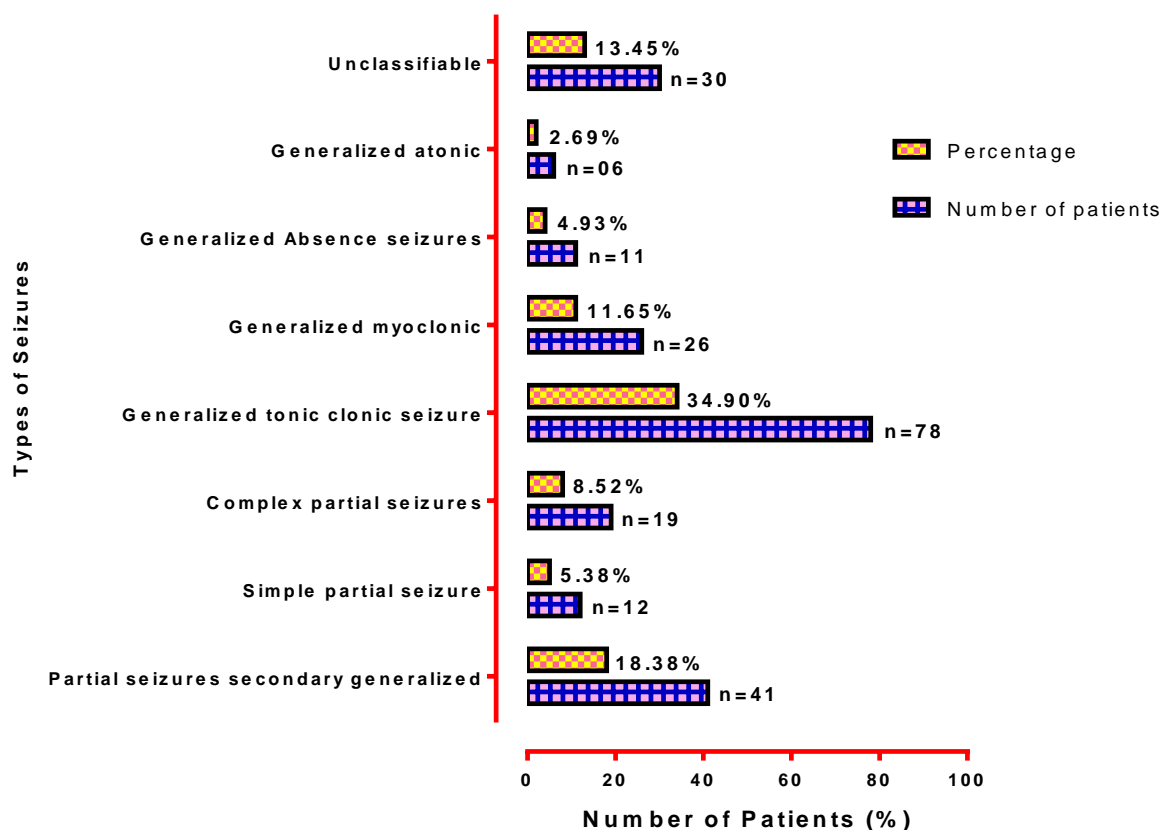


Figure 3: Types of seizures

Table 1: Risk factors among study population

Risk Factors	Number of Patients (n=223)	Percentage (%)
No	65	29.14
Febrile seizure	59	26.45
Head injury	42	18.83
Stroke	26	11.65
Birth trauma	24	10.76
Stress	9	4.03
Brain tumour	3	1.34
Sleep deprivation	8	3.58
Meningitis	6	2.69
Neurosurgery	2	0.89

The results, based on the study of risk factors of epilepsy were shown in figure and 29.14% (n=65) were free from the risk factors, 26.45% (n=59) were having febrile seizures, 18.83% (n=42) were having head injury, 11.65% (n=26) were affected by stroke, 10.76% (n=24) were having birth trauma, 4.03% (n=9) were having stress, 1.34% (n=3) were having brain tumor, 3.58% (n=8) were having sleep deprivation, 2.69% were having meningitis, 0.89% (n=2) were undergone to prior neurosurgery.

**Table 2: Type of therapy**

Prescribing Pattern	Number of Patients (n=223)	Percentage (%)
Monotherapy	101	45.29
Dual therapy	80	35.83
Multiple therapy	42	18.83

Out of 223 respondents antiepileptic monotherapy was observed in 45.29% of all patients, 35.83% people were prescribed with dual therapy (2 drugs) and 18.83% were prescribed with multiple therapies ( $\geq 2$  drugs). Most of the patients are treated and managed with multiple drug therapy and the percentage was 53.81.

**Table 3: Prescribing pattern of antiepileptic drugs among study population**

Drug name	Frequency	Percentage (%)
Sodium valproate	192	86.09
Levetiracetam	38	17.04
Oxcarbazepine	36	16.14
Clobazam	34	15.24
Carbamazepine	15	6.75
Lamotrigine	17	7.62
Piracetam	14	6.27
Phenytoin	10	4.48
Clonazepam	21	9.41
Lobazam	3	1.345
Lonazepam	3	1.345
Gabapentin	2	0.896
Thiopental	4	1.79

Out of 223 respondents, 86.09% of the Epilepsy patients were prescribed with Sodium valproate, 17.04% were prescribed with Levetiracetam, 16.14% were prescribed with Oxcarbazepine, 15.24% were prescribed with Clobazam followed by Carbamazepine (6.75%), Lamotrigine (7.62%), Piracetam (6.27%), Phenytoin (4.48%), Clonazepam (9.41%), Lobazam (1.345%), Lonazepam (1.345%), Gabapentin (0.896%), Thiopental (1.79%). The current study reveals that majority of the patients were prescribed with Sodium valproate (86.09%).

**Table 4: combination of two drug therapy for epilepsy**

Dual Therapy	No of Patients (N=223)	Percentage (%)
Oxcarbazepine+clobazam	5	2.24
Sodium valproate+gabapentin	1	0.44
Sodium valproate+ levetiracetam	18	8.07
Sodium valproate +oxcarbazepine	8	3.58
Sodium valproate + phenytoin	3	1.34
Sodium valproate+carbamazepine	6	2.69
Carbamazepine+ clobazam	1	0.44
Sodium valproate+lorazepam	2	0.89
Sodium valproate +piracetam	5	2.24

Tiopental+ oxcarbazepine	1	0.44
Phenytoin+ clobazam	2	0.89
Sodium valproate+ clonazepam	11	4.93
Oxcarbazepine+levetiracetam	1	0.44
Oxcarbazepine+ pregabalin	2	0.89
Gabapentin+piracetam	1	0.44
Clonazepam+levetiracetam	1	0.44
Sodium valproate+clobazam	11	4.93
Levetiracetam+ phenytoin	1	0.44

Among the study population 30% (n=67) of patients were prescribed with combination of two drug. Sodium valproate and levetiracetam is the most frequently used (n=18, 8.07%) followed by Sodium valproate and clobazam (n=11, 4.93%). In this study two drug combinations have a better production against epileptic patients.

**Table 5: combination of three drug therapy for epilepsy**

Multiple Therapy	No of Patients (n=223)	Percentage (%)
Sodium valproate+levetiracetam+ oxcarbazepine	4	1.79
Sodium valproate+clobazam+oxcarbazepine	3	1.34
Sodium valproate +levetiracetam+clonazepam+ oxcarbazepine	1	0.44
Levetiracetam+clobazam+clonazepam	2	0.89
Sodium valproate+clobazam+ levetiracetam	5	
Sodium valproate+clonazepam+clobazam	2	0.89
Sodium valproate+ oxcarbazepine+ piracetam	2	0.89
Sodium valproate+ levetiracetam+clonazepam	3	1.34
Sodium valproate+clobazam+piracetam	4	1.79
Oxcarbazepine+clobazam+clonazepam	1	0.44
Phenytoin+ clobazam+phenobarbital	1	0.44
Sodium valproate+ clonazepam+ oxcarbazepine	1	0.44
Sodium valproate+carbamazepine+levetiracetam	7	3.13
Clobazam+levetiracetam+piracetam	2	0.89
Sodium valproate+ levetiracetam+ phenytoin	2	0.89
Sodium valproate+carbamazepine+clonazepam	2	0.89

In our study population (n=223), 18.83% of patients were prescribed with triple therapy or multiple drug combinations. Among the study population, most number (n=7, 3.13%) of multiple drug are Sodium valproate , carbamazepine, and levetiracetam combinations, followed by Sodium valproate, levetiracetam and oxcarbazepine, Sodium valproate,clobazam and piracetam (n=4, 1.79%) respectively.

Conclusion:

Prescription patterns were consistent with current evidence about the spectrum of efficacy of individual AEDs in different epilepsy syndromes. The high prevalence of poly therapy, including

combinations of three or more AEDs, is a cause for concern. In our study concluded that the combination therapy may seem costlier than monotherapy in the short term, but when used appropriately, it causes significant savings: lower treatment failure rate, lower case-fatality ratios, and fewer side-effects than monotherapy, slower development of resistance and consequently, less money needed for the development of new drugs.

#### REFERENCE:

1. Theodore WH, Fisher RS. Brain stimulation for epilepsy. *Lancet Neurol.* 2004;3: 111–18.
2. Engel J, et al., Quality Standards Subcommittee of the American Academy of Neurology; American Epilepsy Society; American Association of Neurological Surgeons. Practice parameter: temporal lobe and localized neocortical resections for epilepsy: report of the Quality Standards Subcommittee of the American Academy of Neurology, in association with the American Epilepsy Society and the American Association of Neurological Surgeons. *Neurology.* 2003; 60:538–47.
3. Tsiropoulos I, Gichangi A, Andersen M, Bjerrum L, Gaist D, Hallas J. Trends in utilization of antiepileptic drugs in Denmark. *Acta Neurol Scand.* 2006;113:405–11. Erratum in: *Acta Neurol Scand* 2006; 114: 70.
4. Savica R, Beghi E, Mazzaglia G, Innocenti F, Brignoli O, Cricelli C, Caputi AP, Musolino R, Spina E, Trifirò G. Prescribing patterns of antiepileptic drugs in Italy: a nationwide population-based study in the years 2000–2005. *Eur J Neurol.* 2007;14:1317–21.
5. Perucca E, Berlowitz D, Birnbaum A, Cloyd JC, Garrard J, Hanlon JT, Levy RH, Pugh MJ. Pharmacological and clinical aspects of antiepileptic drug use in the elderly. *Epilepsy Res.* 2006;68(Suppl. 1):S49–63.
6. Forcadas MI, Peña Mayor P, Salas Puig J. Special situations in epilepsy: women and the elderly. *Neurologist.* 2007;6(Suppl. 1):S52–61.
7. Wallace H, Shorvon S, Tallis R. Age-specific incidence and prevalence rates of treated epilepsy in an unselected population of 2,052,922 and age-specific fertility rates of women with epilepsy. *Lancet.* 1998;352:1970–3.
8. Sheorajpanday RV, De Deyn PP. Epileptic fits and epilepsy in the elderly: general reflections, specific issues and therapeutic implications. *Clin Neurol Neurosurg.* 2007;109:727–43.

9. Waterhouse EJ, DeLorenzo RJ. Status epilepticus in older patients: epidemiology and treatment options. *Drugs Aging*. 2001;18:133–42.
10. Brodie MJ, Kwan P. Epilepsy in elderly people. *BMJ*. 2005;331:1317–22.
11. Cloyd J, Hauser W, Towne A, Ramsay R, Mattson R, Gilliam F, Walczak T. Epidemiological and medical aspects of epilepsy in the elderly. *Epilepsy Res*. 2006;68(Suppl. 1):S39–48.
12. Glauser T, Ben-Menachem E, Bourgeois B, Cnaan A, Chadwick D, Guerreiro C, Kalviainen R, Mattson R, Perucca E, Tomson T. ILAE treatment guidelines: evidence based analysis of antiepileptic drug efficacy and effectiveness as initial monotherapy for epileptic seizures and syndromes. *Epilepsia*. 2006;47:1094–120.
13. French JA et al., Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology; Quality Standards Subcommittee of the American Academy of Neurology; American Epilepsy Society. Efficacy and tolerability of the newer antiepileptic drugs I: treatment of newer onset epilepsy: report of the Therapeutics and Technology Assessment Subcommittee and Quality Standards Subcommittee of the American Academy of Neurology and the American Epilepsy Society. *Epilepsia*. 2004;45:401–9.
14. Spina E, Perugi G. Antiepileptic drugs: indications other than epilepsy. *Epileptic Disord*. 2004;6:57–75.
15. Steinman MA, Bero LA, Chren MM, Landefeld CS. Narrative review: the promotion of gabapentin: an analysis of internal industry documents. *Ann Intern Med*. 2006;145:284–93.
16. Steinman MA, Harper GM, Chren MM, Landefeld CS, Bero LA. Characteristics and impact of drug detailing for gabapentin. *PLoS Med*. 2007;4: 134.



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