



## Observational Study on Prescribing Pattern of Antiepileptics in Outpatients in a Neuro-Psychiatric Government Hospital in North India

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### ABSTRACT

Epilepsy is one of the most common neurological disorders characterized by recurrent and unprovoked seizures which are idiopathic. However, its management is symptomatic. New antiepileptic drugs (AEDs) have emerged in the recent years. Investigations of prescribing patterns and exposure of AEDs to different patient groups are important regarding drug safety aspects. So, this study elucidates the prescribing pattern of AED by different neurologists in a Neuro-psychiatric Government Hospital in North India for out-patients considering gender and age differences in prescribing patterns over time. The aim is to explore the prescribing behaviour of antiepileptics by different neurologists of the same Government hospital for out-patients. It was a randomised, observational study carried out in a Neuro-psychiatric Government hospital which comprised of 303 epileptic patients on AEDs who are all in treatment for three months. A data collection form was designed to collect data from out patient's prescription. Sodium Valproate was the most prescribed drug followed by Carbamazepine, Phenytoin. Clobazam was given as an adjuvant therapy in most of the cases. Newer antiepileptics, Levetiracetam and Lacosamide were also given as add-on therapy. One hundred and forty three patients were on monotherapy, one hundred and twenty four were on dual therapy, thirty three on triple therapy and three on four antiepileptics. The study depicted that mono therapy and dual therapy were mostly seen in the hospital than other therapies and Older AEDs were mostly prescribed with benzodiazepines. Uses of Newer AEDs were less.

**Keywords:** Epilepsy, AED – Antiepileptic drug, Observational Study.

### INTRODUCTION

Epilepsy is a group of disorder of Central Nervous System characterized by paroxysmal cerebral dysrhythmia manifesting as brief episodes which we call it as seizures that affects people of all ages. It could be loss or disturbance of consciousness with or without body movements.<sup>1</sup> Episodes of seizures are unpredictable and its frequency highly varies from 1 per year to several per day. An accurate diagnosis of the seizure type and classification is complicated.<sup>2</sup> An eyewitness of a seizure patient is essentially needed for the clinical diagnosis of epilepsy. Neurological examination and investigations may or may not be normal between attacks; seizures might go unnoticed which occurs at night. It adversely affects quality of life and psycho-social status.<sup>3</sup> Mostly all cases of epilepsy are idiopathic but treatment is symptomatic. Antiepileptics suppress and prevent seizures; disease fades out after years of successful control yet there are histories where the disease reappears, which are rare too. Globally, epilepsy has become the most common neurological disorder with approximately 50 million people suffering and it is known that nearly 80% of the people with epilepsy live in developing and poor countries.<sup>4</sup>

There are many antiepileptics, older & newer for the treatment of epilepsy. Older ones include phenytoin, carbamazepine, valproic acid and phenobarbitone which are commonly used as first-line drugs. They are less

costlier than newer antiepileptics like levetiracetam, gabapentin, lamotrigine, vigabatrin, topiramate, lacosamide which are currently used as second-line drugs/add-on/alternative therapy. There are adjuvant therapies to add with older and newer AEDs to subside the frequency of episodic seizures. Each episodic attack of seizure increases the propensity to further attacks. The treatment is initiated with a single drug with low dose, further the level of the dose is increased step by step till the patient gets a complete control of seizures.

Therapeutic Drug Monitoring is a justified guidance for dose adjustments. It is much useful as a therapeutic range of concentration for Older AEDs has been defined and there is a distinct individual variation in the plasma concentration attained with the same dose. If full control is not obtained at maximum tolerated dose of one drug, it is substituted by another drug. Combinations are reasonable when monotherapy fails. Control of seizures are achieved mainly by monotherapy than patients receiving dual or triple therapy of AEDs as it has fewer side effects; lower cost and better tolerability.<sup>5</sup> Moreover, medication adherence and quality of life of epileptic patients with monotherapy are better than patients with dual/triple/polytherapy.

Prescribing pattern of antiepileptics vary for different neurologists across India and do not signify a rational decision making for choosing the drugs. Physicians do not adhere to the guidelines made by regulatory agencies



leading to irrationality and polypharmacy. The treatment of diseases by the use of essential drugs, prescribed by their generic names, has been emphasized by the WHO and the National Health Policy of India.<sup>6</sup>

## MATERIALS AND METHODS

This randomised, observational study was carried out in a Neuro-psychiatric Government hospital in North India. It was carried out over a period of 3 months from December 15, 2015 to March 15, 2016. A total of 303 Out-patients of Neurology Department with a clinical diagnosis of epilepsy meeting the inclusion criteria were enrolled in our study. The demographic details, clinical diagnosis, dose, and frequency of AEDs were recorded in a well designed pro forma. Source of Data Collection was the out-patient prescription which patients receive after consultation to buy medicines. This study primarily aimed at exploring the prescribing pattern of patients who were out-patients and prescribing behaviour in a Government hospital.

## RESULTS AND DISCUSSION

**Table 1:** Types of Therapy

Types of Therapy	Total number	Percentage (%)
Mono therapy (single AED)	142	46.86
Dual therapy (two AEDs)	125	41.25
Triple therapy (three AEDs)	33	10.89
Poly therapy (> 3)	3	0.99

The main aim of treating epilepsy is to control seizure, reduce its frequency and severity. Selection of drug depends on availability, accessibility, efficacy as well as patient factors. Pattern of prescription of antiepileptic do vary in different places within the country and among countries. It also depends according to the different neurologists who prescribe older AEDs, newer AEDs as add-on therapy and benzodiazepines as adjuvant therapy. The total number of prescriptions collected from OP were 303. Our study had 179 males (59.07%) and 124 females (40.62%). Considering the distribution of age, 87 of them in our study were Paediatrics (1-17years), 187 were Adults (18-59years) and 29 were Geriatrics (>60 years). Total AEDs in the study were 504 and they comprised of Older AEDs like Sodium Valproate (56.10%) followed by Carbamazepine (32.34%), Phenytoin (25.08%) and Phenobarbitone (7.59%), Newer AEDs which included Levetiracetam (5.28%) followed by Lacosamide (0.66%) and Benzodiazepines including Clobazam (35.31%) and Clonazepam (3.96%).

Monotherapy with an Older AED is usually given to new-onset of epileptic patients to control seizures. When the patient doesn't get controlled, neurologists either increase the dose of the particular drug or switches on to a Newer AED. Some switch on to benzodiazepines.

The practice of neurologists seen in our study was the addition of a Benzodiazepine, which was mostly Clobazam with an Older AED. 46.86% antiepileptics were prescribed as monotherapy, 41.25% as dual therapy, 10.89% as triple therapy and 0.99% as poly therapy (Table 1).

Sodium Valproate was the commonest monotherapy (56.33%) followed by Carbamazepine (26.76%) and Phenytoin (15.49%) showed in (Table 2).

**Table 2:** AED usage as Monotherapy

AED	Total (142)	Percentage (%)
Sodium valproate	80	56.33
Carbamazepine	38	26.76
Phenytoin	22	15.49
Phenobarbitone	1	0.70
Levetiracetam	1	0.70

The most frequent dual therapy (Table 3) was Sodium Valproate with Clobazam (26.4%) followed by Carbamazepine with Clobazam (20.8%) and Phenytoin with Clobazam (14.4%).

Addition of Sodium Valproate or Carbamazepine or Phenobarbitone with a Newer AED, i.e. Levetiracetam was very few.

In case of Triple Therapy (Table 4), 27.27% of epileptic patients got a combination of Sodium Valproate, Phenytoin and Clobazam and 12.12% with Sodium Valproate, Carbamazepine and Clobazam and 15.15% patients tried on an older AED with a newer AED as add-on therapy and a Benzodiazepine as adjuvant therapy i.e. Sodium Valproate, Levetiracetam and Clobazam.

Polytherapy combinations (>3 AEDs) are shown in (Table 5) below which were too few.

Monotherapy and Dual therapy were frequently prescribed type of therapy in paediatrics and adults while in geriatrics, dual therapy was seen more prescribed followed by monotherapy (Table 6).

In relation to Age & Gender, we could find males were more affected by epilepsy in all age groups than females as well and Adults seem to have affected the most (Table 7).

Majority of the articles assert that young children and elderly people are the most affected and also males are more prone to epilepsy than females.<sup>7</sup>

As the highly accelerated adult sample size was the main limitation of our study, we couldn't come to such conclusion.

Moreover the study was a randomised. In Paediatrics, the most frequently prescribed Monotherapy were Sodium Valproate followed by Carbamazepine and in Dual therapy, Sodium Valproate with Clobazam followed by the same percentage for Carbamazepine with Clobazam



and Phenytoin with Clobazam. In adults, the commonest Monotherapy were Phenytoin followed by Sodium Valproate and in Dual therapy, Sodium Valproate with Clobazam was prescribed frequently followed by Carbamazepine with Clobazam and Phenytoin with Clobazam.

In Geriatrics, monotherapy was Sodium Valproate followed by Carbamazepine. Dual therapy was the combination of Sodium Valproate with Clobazam and

Sodium Valproate with Phenytoin. Triple therapy included a combination of Sodium Valproate, Phenytoin with Clobazam.

Prescribing drugs with generic names is the rationalization of a prescription.

Here, in our study we found that out of 303 prescriptions, monotherapy and dual therapy was prescribed in generic names in 189 and 65 prescriptions respectively. 41 prescriptions used Brand names of AEDs (Table 8).

**Table 3:** AED usage as Dual Therapy

AED	Total (125)	Percentage (%)
Sodium valproate + clobazam	33	26.4
Carbamazepine + clobazam	26	20.8
Phenytoin + clobazam	18	14.4
Sodium valproate + carbamazepine	12	9.6
Phenytoin + carbamazepine	5	4
Phenytoin + phenobarbitone	5	4
Sodium valproate + phenytoin	5	4
Sodium valproate + levetiracetam	5	4
Sodium valproate + clonazepam	5	4
Carbamazepine + phenobarbitone	4	3.2
Sodium valproate + phenobarbitone	3	2.4
Phenobarbitone + levetiracetam	1	0.8
Phenytoin + clonazepam	1	0.8
Carbamazepine + levetiracetam	1	0.8
Phenobarbitone + clobazam	1	0.8

**Table 4:** AED usage as Triple Therapy

AED	Total (33)	Percentage (%)
Sodium valproate + phenytoin + clobazam	9	27.27
Sodium valproate + levetiracetam + clobazam	5	15.15
Sodium valproate + carbamazepine + clobazam	4	12.12
Phenytoin + phenobarbitone + clobazam	3	9.09
Carbamazepine + phenobarbitone + clobazam	2	6.06
Sodium valproate + clobazam + clonazepam	2	6.06
Carbamazepine + phenytoin + clobazam	2	6.06
Sodium valproate + carbamazepine + phenytoin	1	3.03
Sodium valproate + phenytoin + levetiracetam	1	3.03
Carbamazepine + levetiracetam + clobazam	1	3.03
Sodium valproate + phenobarbitone + levetiracetam	1	3.03
Sodium valproate + phenytoin + phenobarbitone	1	3.03
Sodium valproate + carbamazepine + phenobarbitone	1	3.03

**Table 5:** AED usage as Polytherapy

AED	Total (3)	Percentage (%)
Sodium valproate + phenytoin + clobazam + clonazepam	1	33.33
Carbamazepine + phenytoin + lacosamide + clobazam	1	33.33
Sodium valproate + carbamazepine + lacosamide + clobazam	1	33.33



**Table 6:** According to Age & Gender Distribution

Age Distribution	Therapy *(M,D,T,P)	Total No.	Percentage (%)
<b>Paediatrics (n=87)</b>	M	43	49.42
	D	37	42.52
	T	5	5.7
	P	2	2.2
<b>Adults (n=187)</b>	M	87	46.52
	D	76	40.64
	T	23	12.29
	P	1	0.53
<b>Geriatrics (n=29)</b>	M	11	37.93
	D	15	51.72
	T	3	10.34

\*M= Monotherapy, \*D= Dual therapy, \*T= Triple therapy, \*P= Polytherapy

**Table 7:** Distribution of AEDs according to type of therapy in relation to gender

<b>Paediatrics (male=54 ; female=33)</b>		
Type of Therapy	Total male N (%)	Total female n (%)
<b>Most frequent monotherapy</b>		
Sodium valproate (n=24)	16 (66.66)	8(33.33)
Carbamazepine (n=16)	7(43.75)	9(56.25)
<b>Most frequent dual therapy</b>		
Sodium valproate + clobazam (n=9)	5(55.55)	4(44.44)
Carbamazepine + clobazam (n=9)	5(55.55)	4(44.44)
Phenytoin + clobazam (n=8)	6(75)	2(25)
<b>Adults (male=107 ; female=80)</b>		
<b>Most frequent monotherapy</b>		
Sodium valproate (n=46)	27(58.69)	19(41.30)
Carbamazepine (n=20)	9(45)	11(55)
Phenytoin (n=19)	12(63.15)	7(36.84)
<b>Most frequent dual therapy</b>		
Sodium valproate + clobazam (n=18)	11(61.11)	7(38.88)
Carbamazepine + clobazam (n=15)	4(26.66)	11(73.33)
Phenytoin + clobazam (n=10)	6(60)	4(40)
<b>Most frequent triple therapy</b>		
Sodium valproate + phenytoin + clobazam (n=6)	6(100)	0
<b>Geriatrics (male=18 ; female=11)</b>		
<b>Most frequent monotherapy</b>		
Sodium valproate (n=9)	5(55.55)	4(44.44)
Carbamazepine (n=2)	1(50)	1(50)
<b>Most frequent dual therapy</b>		
Sodium valproate + clobazam (n=6)	5(83.33)	1(16.66)
Sodium valproate + phenytoin (n=4)	3(75)	1(25)
<b>Most frequent triple therapy</b>		
Sodium valproate + phenytoin + clobazam (n=3)	1(33.33)	2(66.66)

**Table 8:** No. of prescriptions containing AEDs in generic name

No. of AEDs in Generic	No. of Prescriptions	Percentage (%)
AEDs in brand names	41	13.53
1 AED in generics	189	62.37
2 AEDs in generics	65	21.45
3 AEDs in generics	7	2.31
4 AEDs in generics	1	0.33

**CONCLUSION**

In conclusion, the prescription pattern of different neurologists is typically different in prescribing AEDs to different epileptic patients. Limitations of this study need to be considered. Firstly, diagnoses made by the neurologists did not determine the different subtypes of epilepsy and so we couldn't evaluate the AED use for treatment of epileptic patients. Secondly, as our results are restricted to an outpatient setting, equal number of people in certain age group (children, adults & elderly) couldn't be taken as such, as highly affected (children & elderly) were more likely to be admitted to these facilities. However, this study was aimed to explore the prescribing pattern of AEDs without considering any clinical outcome. Our findings could not be fully generalized to the whole general practice of neurologists all over India.

Monotherapy is usually the ideal and preferable choice over polytherapy whenever possible in epilepsy care. When seizure doesn't get controlled, dual therapy/triple therapy/polytherapy comes to help. It could be the addition of a Benzodiazepine or a Newer AED as per the habit of prescribing of a particular neurologist. When a patient becomes seizure-free while receiving polytherapy/triple therapy, dose of the drug needs to be tapered gradually and discontinue the baseline AED which has been previously ineffective or poorly tolerated.

The lack of knowledge of epilepsy, need of treatment at the apt time, factors like poverty, cultural beliefs, stigma, poor health infrastructure, and shortage of trained professionals contribute for the treatment gap which

accelerates the statistics of epilepsy in India. Infectious diseases also play an important role in seizures and long-term burden causing both new-onset epilepsy and status epilepticus. Proper education and empowerment of health care services can make tremendous change in a developing country like India. The yoke of epilepsy could be reduced in India by alleviating poverty and by reducing the preventable causes like perinatal insults, parasitic diseases, and head injuries.

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