# Prescription pattern in epilepsy in peadiatric age group in tertiary care teaching hospital

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## ABSTRACT

*Epilepsy is a prevalent chronic neurological disorder in peadiatric population and Anti-epileptic Drugs (AEDs) have a narrow margin of safety. The aim of this study was to analyse use of various AEDs and type of epilepsy prevalent in our population. In this study prescriptions for epilepsy from paediatric outpatient department, over five month period (from January 2015 to May 2015) were retrospectively analysed.*

*Total of 160 prescreptions were analysed. 95 (59.3%) were female and 65 (40.7%) were males. 70 (43.8%) patient belonged to 11-15 years of age group, 49 (30.6%) patient belonged to 6-10 years age group, 41 (25.6%)patient belonged to 0-5 years age group. Generalised Tonic Clonic Seizure (GTCS) was the most common diagnosed epilepsy (61.5%), followed by Partial seizure (30.6%) and Absence seizure (8.5%). 117 (73.1%) patient were prescribed monotherapy whereas polytherapy were given to 4 (2.5%) patient. 39 (25%) patient were given two drug combination. Sodium valproate was commonest monotherapy (53%) followed by Carbamzepine (29.9%), Phenytoin (8.5%) and Phenobarbitone (8.5%). Sod. Valproate with Phenytoin was commonest prescribed two drug combination (48.7%) followed by Sodium valproate with Phenobarbitone (28.2%). Among polytherapy Sodium valproate with Phenytoin and Levetiracetam were given to 3 patient.*

*In this study GTCS was most common diagnosis and conventional AED were commonly used. Sod. valproate was commonest prescribed AED as monotherapy and in combination therapy .*

**Keywords:** *Epilepsy, Anti-epileptic Drug (AED), Generalised Tonic Clonic Seizure (GTCS), Prescription pattern, Tertiary care hospital*

## INTRODUCTION

An epileptic seizure is a transient paroxysm of uncontrolled discharges in neurons and a medical condition with recurrent, unprovoked seizures.[1] Epilepsy is a common pediatric problem and approximately 6-7% of children suffer at least one or more epileptic seizures.[2]There are several prevalence studies however and a recent meta-analysis suggest that the prevalence rate is 5.59 per 1000 population with no gender and geographical differences.[3] This rate is surprisingly similar to the rate in developed country. Children with epilepsy are prescribed antiepileptic medication with the aim of control of seizures, minimum drug side effects and improved quality of life.[4,5]

As most of the antiepilepticdrugs have a narrow therapeutic and safety margin, high doses of antiepileptic drugs can lead to side effects, on theother hand suboptimal doses will lead to recurrence of seizures. Also, wrongly chosen drugs result in poor controlof epilepsy or sometimes increase in seizures frequency.

The choice of most appropriate antiepileptic drug (AED) depends on classification of seizures and age of patient.[5,6] Seizure control may be achieved by monothearpy in about 80% of the patients, with the other 20% requiring two to three AEDs.[7] Monotherapy is normally the first line of treatment, as it has less drug interactions and side effects; lower cost, better tolerability, medication adherence, and quality of life but polytherapy is often required for patients with multiple seizure types or refractory disease.[8]

A large number of drugs are currently available for the treatment of epilepsy. Conventional drugs like Phenytoin, Carbamazepine, Sodium valproate and Ethosuximide are commonly used as first line drugs. They are relatively less expensive than the newer antiepileptic drugs like Gabapentin, Lamotrigine, Vigabatrin, Topiramate, Tiagabine and Zonisamide. They have lesser adverse effects and have a few drug interactions.[9,10]

Whenchoosing an AED, factors such as mechanismof action, ease of dosing, efficacy, long term adverse effects, neuropsychiatric profile, sedative burden, interaction with other medications, seizuretypes and other co-morbid conditions should be considered.[11,12] Usage of AEDs differs in different geographical regions, depends partly on economic status and drug availability.

The aim of this study was to analyse use of various AEDs and type of epilepsy prevalent in our population.

## MATERIALS AND METHODS

This retrospective analytical study was carried out in Dr. Bhim Rao Ambedkar hospital, Raipur (C.G.) associated with Pt JNM Medical college, Raipur(C.G.). Permission was obtained from institutional ethical committee. All prescription, over 5 month period (January 2015 to May 2015) for epilepsy from peadiatric out patient department were collected and analysed as per WHO guideline" How to investigate drug used in health facilities".[13] Diagnosis was confirmed by two peadiatrician based on the clinical presentation of seizures, Electroence-phalogram (EEG) and scan test.

Patients demographic details, clinical diagnosis, type of epilepsy, type of AED used, drug dose and frequency were recorded. Drug used as oral or parenteral were noted.Average number of drug per prescription were calculated. Other co-prescribeddrug were noted.The epileptic seizures were categorized according to the classification of international league against epilepsy.[14]However, patients having more than one type of seizures were categorized as unclassified seizure or mixed type of seizure.The patients were further classified in to different age group: 0-5, 6-10, 11- 15, 16- 18 years. According to numbers of drug prescribed, patients were grouped as monotherapy, two-drugcombination and polytherapy. The patients using three or more drug were classified as polytherapy. Phenytoin, Carbamazepine, Sodium valproate, Phenobarbitone were categorized as conventional AED. Levetiracetam, Topiramate, Zonisamide as newer AED. Various other similar studies on this subject were studied and compared with prescription of this study.

## RESULTS

Total 160 prescriptions were analysed. 95 female and 65 male (figure -1). 70 patients were age group of 11- 15 year, 49 patients of 6-10 year and 41 patients of 0-5 year(figure-2). GTCS was more common diagnosis 98, partial seizure 49, absence seizure 10 and unclassified seizure 3(figure-3). 117 (73.1%) were on monotherapy, 40 (25%) were taking two-drug combination therapy, 4 (2.5%) were prescribed polytherapy. Sodium valproate was the commonest monotherapy 62 (53%), followed by Carbamazepine 35(29.9%), Phenytoin 10(8.54%), and Phenobarbitone 10 (8.54%) (table-2).

Sodium valproate with Phenytoin was most frequent 2-drug combination (19), followed by Sodium valproate with Phenobarbitone (11), Sodium valproate with Carbamazepine (5), Carbamazepine with Phenytoin (2)(table-3). Sodium valproate, Phenytoin with Leviteracetam were commonestpolytherapy (table -4). Other type of combinations are shown in table 3 and 4.

Oral route were preferred in all patients, parenteral drug was not given to any patient. 66 patients were given Calcium supplement, B-complex 31, Multi-vitamin 21, Folic acid18, Cough syrup 14, Colecalciferol sachet 10.Paracetamol, Amoxicillin, Albendazole, Diclofenac sodium, Pantoprazole were other co-prescribed drugs (table-8). Average number of drug per prescription was 2.41.

**Table 1: AEDs used in this study**

| "Conventional" AEDs | "Newer" AEDs | Benzodiazepine |
|---|---|---|
| Sodium valproate<br>Carbamazepine<br>Phenytoin<br>Phenobarbitone | Levetiracetam<br>Topiramate | Clobazam |

**Table 2: Monotherapy**

| Drugs | Total=117 | % |
|---|---|---|
| Sod. Valproate | 62 | 53 |
| Carbamazepine | 35 | 29.9 |
| Phenytoin | 10 | 8.5 |
| Phenobarbitone | 10 | 8.5 |

**Table 3: Two-drug combination**

| Drugs | Total = 40 | % |
|---|---|---|
| Sod. Valproate + phenytoin | 19 | 48.7 |
| Sod. Valproate + phenobarbitone | 12 | 28.2 |
| Sod. Valproate + carbamazepine | 5 | 12.8 |
| Phenytoin + phenobarbitone | 1 | 2.6 |
| Carbamazepine + levoteracetam | 2 | 5.1 |
| Carbamazepine + topiramate | 1 | 2.6 |

**Table 4: Polytherapy**

| Drugs | Total = 4 | % |
|---|---|---|
| Sod. Valproate + phenytoin + levoteracetam | 3 | 75 |
| Sod. Valproate + phenobarbitone + phenytoin | 1 | 25 |

**Table 5: Co-prescribed drugs**

| Drugs | Number |
|---|---|
| Calcium | 66 |
| B-complex | 31 |
| Multi-vitamin | 21 |
| Cough syrup | 14 |
| Colecalciferal sachet | 10 |
| Paracetamol | 5 |
| Amoxicillin | 4 |
| Albendazole | 3 |
| Diclofenac sodium | 3 |
| Pantoprazole | 2 |

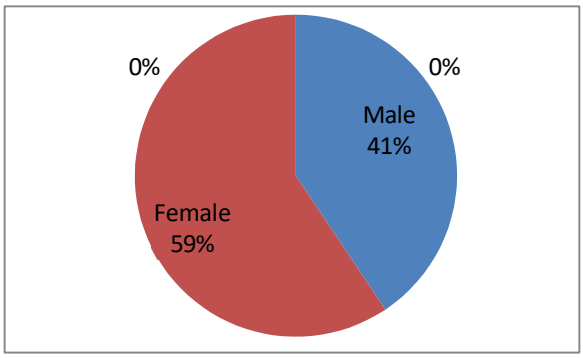


**Fig. 1: Graphical presentation of the distribution of 160 epileptic patients based on the gender**

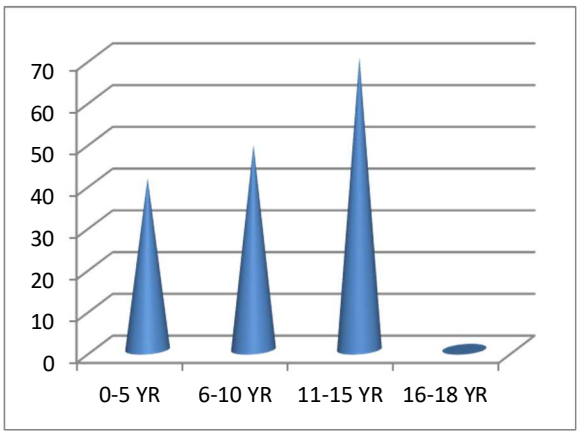


**Fig. 2: Graphical presentation of the distribution of age group with number of patients**

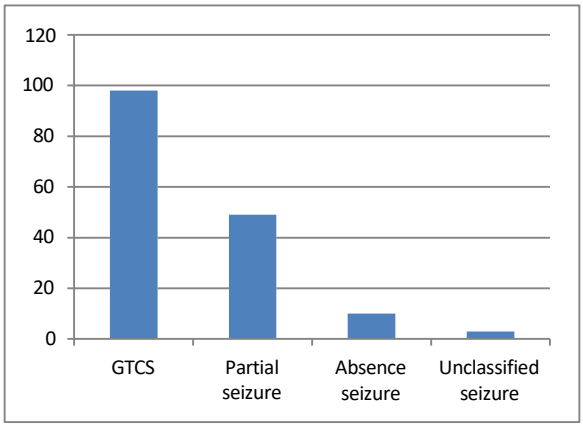


**Fig. 3: Graphical presentation of the distribution of type of seizure with number of patients**

## DISCUSSION

In this retrospective analytical study 160 prescriptions for epilepsy in peadiatric patients were analalysed. It was found that higher percentage of patients were female (59.3%) than male patients (40.7%). Various epidemiological studies on epilepsy are unable to explain a differences in gender distribution in their study population.[11,15,16] And some study describe a female preponderance.[15,17] Though reasons behind gender differences are not clear but it suppose that estrogen has seizure activating effect.[18] Maximum patient in this study were of age group 11-15 years(43.8%) followed by 6-10 years (30.6%) and 0-5 years (25.6%). According to literature, the incidence of epilepsy has bimodal distribution with peak in 1st decade and a second peak in elderly.[19,20,21]

A higher percentage of patient were found to have GTCS(61.53%), as in other study done by sachchidanad Pathak et al. [22]30.6% patients were have partial seizure, absence seizure were 8.5%. However the type of epilepsy could not be identified in 3 patients. In this study most of the patients were prescribed monotherapy (73.1%) whereas polytherapy were given to only 2.5% of patients. Like earlier studies.[22,23,24] 25% of patients were used two drug combination therapy. Polytherapy may leads to increase in side effects, drug interactions and adversely affect quality of life.[25,26,27] Nevertheless multiple drug therapy is unavoidable in some resistant cases, monotherapy in its higher tolerated dose not only can control epilepsy but also reduces occurrence of convulsion frequency and increases compliance.[11,12]

Despite availability of Various newer AED with equal effectiveness and better tolerability, conventional AEDs were mostly prescribed. It may be due to low cost.[22] Availability in government supply as these are included in Essential Drug List (EDL).[28] and ability to effectively control seizure. But higher propensity to cause side effect is matter of concern.[24]

Among conventional AED, Sodium valproate was most commonly preferred AED as monotherapy(53%), followed by Carbamazepine (29.9%), Phenytoin(8.5%) and Phenobarbitone (8.5%). This was in contradiction withearlier study by Shih-Hui et al[23], where Carbamazepine was found to be most commonly used AED as monotherapy. In another study done by Juny Sebastian et al [29] Phenytoin was most commonly used AED as monotherapy (41.7%) followed by Valproate(41%). Whereas, like this study, sachchidanadpathak et al.[22] found, Sodium valproateas most commonly used AED as monotherapy. Sodium valproate was also more commonly used in two drug combination therapy and in polytherapy as well. Due to its broad spectrum of activity, Sodium valproate was used to control most of the GTCS, partial seizure and absence seizure. Newer AED were not commonly prescribed. May be due to higher cost[22] and nonavailablity in government supply, as they are still not included in EDL.[28]Levetiracetam and Topiramate are newer AED used in this Study.

Amongs two drug combination therapy, Sodium valproate with Phenytoin was most commonly used (47.5%) followed by Sodium valproate with Phenobarbitone(30%) and Sodium valproate with Carbamazepine (12.5%). Unlike

earlier study, where Phenytoin with Phenobarbitone was most commonly used two drug combination therapy.[29] Amongspoly therapy, Sodium valproate with Levetiracetam and Phenobarbitone were given to 3 patients followed by Sodium valproate with Phenytoin and Phenobarbitone (1). Clobazam a Benzodiazepine was used as adjuvant to Sodium valproatein 3 patients with GTCS. Oral route was preferred in all the patients for drug administration. Because oral administration is easy and painless.

Calcium was the most common co-prescribed drug 66 (42.1%), followed by B-comlex 31(19.4%), Multi-vitamin 21(13.1%) and Folic acid 18(11.3%) (table-5). Some antiepileptic drugs specially Phenytoin, interferes with calcium and vitamins absorption and metabolism, and are prone to cause side effect like Osteomalacia and Megaloblastic anaemia.[30]

## CONCLUSION

To conclude, GTCS was the most common diagnosis and monotherapy was preferred modality of treatment. Most commonly used AED as monotherapy was Sodium valproate followed by Sodium valproate with Phenytoin in combination therapy. It was concluded that Prescription pattern in this study is relevant with current trend of prescription pattern.

However our study was limited to single hospital with limited number of patients and was designed to limited duration of time.

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Peadiatric department, Dr BRA Hospital, Raipur (C.G.).

## Bibliography

1. Helms, Quan, Herfindal, Gourley. Textbook of therapeutics: drug and disease management: 8th edition.2006. Seizure disorder. Chap 62; 1609-1611.
2. Major P, Thiele EA. Seizures in Children; Determining the Variation. Pediatrics in Review .2007; 28 (7): 363 - 371
3. Shridharan R, Murthy BN, Prevalence and pattern of epilepsy in india. Epilepsia 1999;40 (5):631-636
4. Palanisamy A, Sankaravadivu T, Subasini U, Narmadha MP, Rajendran NN. Antiepileptic drugs and cognitive impairment in epileptic patients at a private hospital. *Research J PharmaceuticalBiological & Chemical Sciences (RJPBCS)* 2011; 2(3):824-9.
5. Uiji SG, Uiterwaal CS, Aldenkamp AP, *et al*. Adjustment of treatment increases quality of life in patients with epilepsy: a randomized controlled pragmatic trial. *EurJNeurol*2009; 16: 1173-7.
6. Bielen I, Sruk A, Planjar-Prvan M, *et al*. Age-related antiepileptic drug utilization in active epilepsy: A population based survey. *CollAntropol*2009; 33(2):659-63.
7. Arul Kumaran KSG, Palanisami S, Rajasekharan A. A study on drug use evaluation of anti epileptics at a multi specialty tertiary care teaching hospital. *IntJ Pharm Tech Res* 2009; 1(4):1541-7.
8. Dhillon S, Sander JW. Epilepsy. Clinical pharmacy and therapeutics. China: Churchill Livingstone; 2007. p.447-60.
9. Cloyd JC, Remmel RP. Antiepileptic drug pharmacokinetics and interactions: Impact on treatment of epilepsy. Pharmacotherapy 2000; 20 (8 Pt 2):139S-151S.
10. Foletti GB. Clinical utilization of new anti-epileptic agents. Rev Med Suisse Romande 2000 Sep; 120(9):703-7.
11. Ochoa JG, Riche W. Antiepileptic drugs. E medicine. medscape.com 2009; 1-39.
12. Clinical Practice Guidelines. Epilepsy in adults. Singapore Epilepsy Society 2007;1-51
13. WHOHow to Investigate Drug Use in Health Facilities: Selected Drug Use Indicators - EDM Research Series No. 007. Accessed online on 12 july 2015
14. Tsiropoulos B, Gichangi A, Anderson M et al."Trends in utilization of antiepileptic drugs in Denmark"; ActaNeurologicaScandinavica, 2006,113,405-411
15. Arul Kumaran KSG, Palanisami S, Rajasekharan A. A study on drug use evaluation of anti epileptics at a multi specialty tertiary care teaching hospital. *IntJ Pharm Tech Res* 2009; 1(4):1541-7.
16. Kariyawasam SH, Bandara N, Koralagama A, Senenayake S. Challenging epilepsy with anti epileptic pharmacotherapy in a tertiary care teaching hospital in SriLanka. *Neurol India* 2004; 52(2): 233-7.
17. Huying F, Klimpe S, Werhan KJ. Anti epileptic drug use in nursing home residents: A cross sectional, regional study. *Seizure* 2006; 15: 194-7
18. Susan J, Rogers, Jose E, Cavazos. "Pharmacotherapy". Epilepsy; 7th edition: page 928-949
19. Caprio A, Hauser WA. Epilepsy in the developing world. *CurrNeurolSci Rep* 2009; 9(4):319-26.
20. Hanssen Y, Dulue D, Al Balushi K, Al Hashar A, Al Zakwani I. Drug utilization pattern of anti-epileptic drugs: a pharmacoepidemiologic study in Oman. *Journal of ClinicalPharmacy and Therapeutics* 2002; 27:357-64
21. Lim SH, Tan EK. Pattern of antiepileptic drug usage in a tertiary referral hospital in Singapore. *Neurol JSoutheast Asia* 1997; 2:77-85.
22. Sachchidanand Pathak, Lalit Singh, Tanuja Singh, S.K. Sharma**, "**Prescribing patterns of Anti-epileptic drug in different age group in India". *Journal of Drug Discovery and Therapeutics;2013,* 1 (7), 69-75
23. Shih-HuiLM,Eng-King TAN, Christopher CHEN. "Pattern of anti-epileptic drug usage in a tertiary referral hospital in Singapore"; *Neurol J Southeast Asia; 1997; 2 : 77-85*
24. Sandeep A, Surya Chandra D, Bhanu Chand T, Saravanan S, Saravanan Kumar R.T., "Study of drug utilization, cost-effectiveness and outcome, of Antiepileptics used in paediatric ward of tertiary care hospital in Tamilnadu, India"; international journal of pharmaceutical research scholer;2013, 2(4), 490-502.
25. Vazquez B. Monotherapy in epilepsy role of the newer antiepileptic drugs. *Arch Neurol*2004; 61(9):1361-5.
26. Thomas SV, Koshy S, Sudhakaran Nair CR, Sarma SP. Frequent seizures and polytherapy can impair quality of life in persons with epilepsy. *Neurol India* 2005; 53(1):46-50.
27. Elliot R. Geriatic pharmacy practice. In: Parthasarathi G, Hansen KN, Nahata MC, eds: A text book of clinical pharmacy practice- essential concepts and

skills. 1st ed. Chennai: Orient Longman Private Limited, 2004:190-217.

28. Essential Drug List C.G.(EDL-13), online www.cghealth.nic.in. accessed online on 20 july 2015
29. Juny Sebastian , R Adepu ,BS Keshava,SHarsha "Assessment of antiepileptic drugs usage in a South Indian tertiary care teaching hospital**"** *Neurology Asia 2013; 18(2) : 159 – 165*
30. James O, McNamara; Pharmacotherapy of Epilepsies; "Goodman& Gilman's- The Pharmacological Basis of Therapeutics" ; . Chap-21; 12th edition; p-593.