

An Analysis of Prescription Pattern of Antiepileptic Drugs in a Pediatric Population of Tertiary Care Teaching Hospital

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Conflict of interest: Nil

Abstract

Background: Prescription pattern of drugs plays a important role in helping the health care system to understand, interpret and improve the prescribing administration and using medications. Without the knowledge of how drugs are being prescribed and used in children with epilepsy, it is difficult to initiate discussion on rationale drug use and to suggest measures to change prescribing habits for the better management.

Aims and Objectives: To study prescribing patterns of antiepileptic drugs (AEDs) in pediatric patients along with the assessment of effectiveness, compliance and safety profile of AEDs in tertiary care teaching hospital.

Methodology: This was a prospective, observational, single center study conducted at Pediatrics department of tertiary care teaching hospital in Gujarat from August 2019 to July 2020. Prescriptions of patients attending pediatric outpatient and inpatients department were collected prospectively. The particulars of the participants were collected at the time of enrollment comprised of baseline demographics data, type(s) of seizures, characteristics of the disease, existing drug therapy (dose and duration), and any other concurrent medications during the study. All data were recorded on case record forms and analyzed using descriptive statistics.

Result: A total of 599 prescriptions were collected, male female ratio being 1.6:1. Most common pediatric age group diagnosed with epilepsy was less than 5 years of age. Duration of epilepsy was between 1 to 5 years in 63.7% of patients. In the pediatric patients of above 3 years age group, schooling was compromised because of epileptic disease. EEG was advised to 17% of patients and MRI to 3.8% of patients. Generalized epilepsy was the most common type of epilepsy observed in 46.2% of patients followed by focal Epilepsy in 25.2% of patients. Most common AED prescribed was sodium valproate in 57.9% prescriptions and 24.7% patients were prescribed with carbamazepine. Average number of drugs prescribed per patient was 1.56. Sodium valproate in generalized seizure patients and carbamazepine in focal epilepsy patients most commonly prescribed AEDs. After 6 months of therapy, seizure free patients with valproate were 58%, with carbamazepine were 75% and with levetiracetam were 20%. Total 61.1 % patients were seizure free. Lowest dose of all the AEDs achieved max seizure free patients and highest doses were less effective.

Conclusion: Generalized tonic clonic seizure was the most commonly observed type of seizure and sodium valproate was the most frequently prescribed drug to them followed by focal seizure. Most common drug prescribed to patients with focal seizure is carbamazepine. Majority of patients were given monotherapy to achieve seizure control. Reduction in seizure episodes was noted with all the drugs and doses but highest seizure free patients were observed with lowest doses of AEDs. The higher doses were found less effective reason for which needs to be explored.

Keywords: Antiepileptics Drugs, Pediatric, Seizure, Monotherapy,

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Background

WHO defines drug utilization in 1977 as “the marketing, distribution, prescription and use of drug in a society with special emphasis on resulting medical, social and economic consequences” [1]. It plays a significant role in helping the health care system to understand, interpret and improve the prescribing administration and using medications [2]. Without the knowledge of how drugs are being prescribed and used in children with epilepsy, it is difficult to initiate discussion on rationale drug use and to suggest measures to change prescribing habits for the better management.

Epilepsy is one of the most common neurological disorders in children characterized by recurrent episodic paroxysmal involuntary clinical events associated with abnormal electrical activity from the neurons [3]. Among the population with newly diagnosed epilepsy, children and older adults are the most rapidly growing segments [4]. Despite the increase in the number of antiepileptic drugs (AEDs), more than 30% of children with childhood epilepsy continue to have seizures even [5]. The incidence is highest in children below 3 years of age, with a decreasing frequency in older children [6]. There are number of pharmaco-epidemiological studies that have reported a budding trend in use of AEDs, especially in refractory patients [7]. The introduction of newer AEDs resulted in an increase in the potential for polytherapy regimens. Consultants treating pediatric epileptic patients are challenged due to lack quality data on AED choice [8].

The main goals of epilepsy therapy include complete seizure control, no adverse side effects, and patients to be seizure-free throughout the rest of their lives [9].

However, the outcome of AED therapy in children depends on many factors, including selection, dosing and monitoring of AEDs, the identification of underlying cause, the type of seizures and the pharmacokinetic parameters of AEDs. [2]. All these factors are essential for successful management, but there is a lack of properly conducted outcome-based studies in pediatrics.

The aim of the present study was to determine prescribing patterns of AEDs in pediatric patients along with the assessment of effectiveness of therapy, compliance and safety profile of AEDs in tertiary care hospital of Gujarat.

Methods

This was a prospective, observational, single center study conducted at Pediatrics department of tertiary care teaching hospital in Gujarat from August 2019 to July 2020. The study was approved by Departmental Screening Committee and Institutional Ethics Committee. The study was conducted as per the guidelines of Indian Good Clinical Practice (GCP) as harmonized with ICH-GCP guidelines. The treatment protocol of the patients remained unaffected by participation in the study. Inclusion criteria were patients of age <15 years and both gender diagnosed with epilepsy, receiving at least one AED, and attending pediatric outpatient or inpatient department for general follow-up visits during study period. Patients not willing to be part of the study or refusing to sign Informed Consent Form were excluded from study. Before collection of the data, informed signed consent form was obtained from the child’s legal guardians. The patients were also provided the patient information sheet to understand the study procedure and study related

details. A suitable case record form was designed to collect all the necessary and relevant information.

The particulars of the participants were collected at the time of enrollment comprised of baseline demographics data, type(s) of seizures, characteristics of the disease as per ILAE [10], existing drug therapy (dose and duration), and any other concurrent medications during the study. All data were recorded on hard copy and then subsequently entered in the electronic platform. The recorded data were analyzed in Microsoft Office Excel-2013 and using descriptive statistics.

Results

Total of 599 epileptic children of both sexes were included for the study among which 566 were from outpatient department and 33 were from indoor department. In this study maximum number (75.5%) of patient belongs to less than 5 years of age group, patient 5 to 10 years of age group were 24.2% and 0.3% patients were greater than 10 years age group. Out of 599 patients, 62.1% patients were male whereas 37.8 patients were female with male to female ratio of 1.6:1 (figure 1).

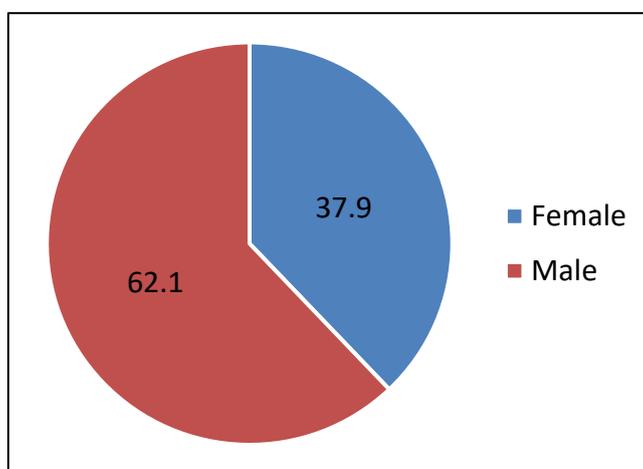


Figure 1: Gender wise distribution

Majority of the patients (67.3%) had disease duration of 1-5 years while 5.3% patients had new onset of disease as defined in figure 2. In educational status among children of 3 years or greater than that, 45.5% were attending school regularly and 54.5% patients were not able to attend school regularly. For investigational purpose, EEG was done in 17% patients and MRI in 3.8% patients.

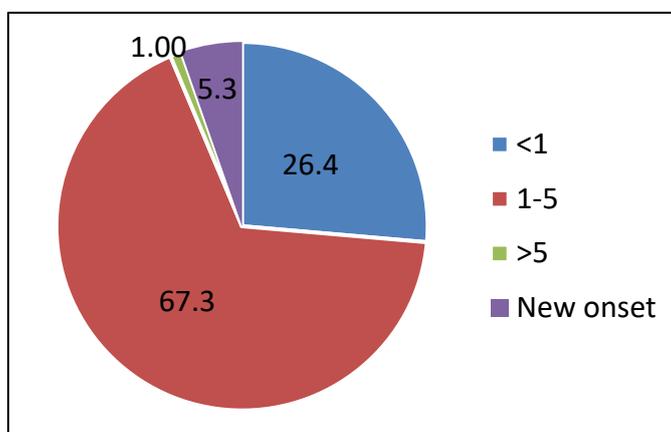


Figure 2: Distribution of patients according to duration of disease

Total number of patients having generalized epilepsy were 277 (46.2%), Focal epilepsy in 151(25.2%), Remote symptomatic epilepsy in 58(9.68%), Myoclonic seizure in 8(1.3%), Absence seizure in 7(1.17%). Remaining were temporal lobe epilepsy, epilepsy due to congenital rubella syndrome, cerebral palsy with generalized seizures, newer onset seizures and febrile seizures.

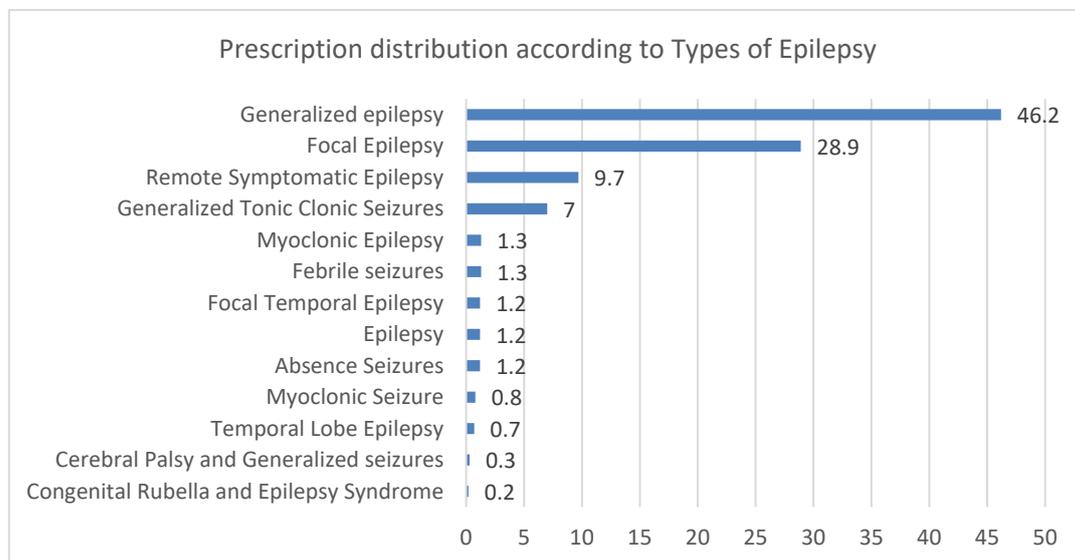


Figure 3: Distribution of patients according to type of epilepsy

Total 95.83% drugs were prescribed from NLEM, 2015 while 5.13% were Non-Essential medicines which were also prescribed as add on therapy. Valproate and Carbamazepine were the most commonly prescribed AEDs in 57.9% and 24.7% patients respectively. Levetiracetam was given to 5.5% patient and other drugs prescribed were Phenobarbitone, Clobazam, Diazepam, paracetamol, Clonazepam, Fosphenytoin, Topiramate, lamotrigine and Zonisamide. (Table 1) The average number of drugs prescribed to every patient was 1.21.

Table 1: Number of antiepileptic prescriptions with Essential drugs as per NLEM, 2015

Drug Type	Drug	ATC code	Frequency	Percent	Total
Essential drug	Valproate	N03AG01	422	57.9	94.90%
	Carbamazepine	N03AF01	180	24.7	
	Levetiracetam	N03AX14	40	5.5	
	Phenobarbitone	N03AA02	18	2.5	
	Clobazam	N05BA09	12	1.6	
	Diazepam	N05BA01	9	1.2	
	Paracetamol	N02BE01	7	1.0	
	Clonazepam	N03AE01	3	.4	
Non-Essential drug	FosPhenytoin	N03AB05	25	3.4	5.10%
	Topiramate	N03AX11	7	1.0	
	Lamotrigine	N03AX09	4	.5	
	Zonisamide	N03AX15	1	.1	

The most common drug prescribed to generalized seizure patient was valproate (45%) and to patients with focal epilepsy was carbamazepine (23.8%). All the myoclonic epilepsy patients were prescribed valproate and clobazam most. Absence seizure patients were prescribed sodium valproate, clonazepam and zonisamide along with sodium valproate.

Nearly half of the patients (49.5%) had 1-2 seizures per month. Others 41.1% had 3 to 4 seizures and 6.3% had 6-8 episodes per month before initiation of AEDs. After 6 months of therapy, 61.1 % patients were seizure free, 34.7 % had 1-2 episodes and only 4.2% patients had 3-4 episodes per month.

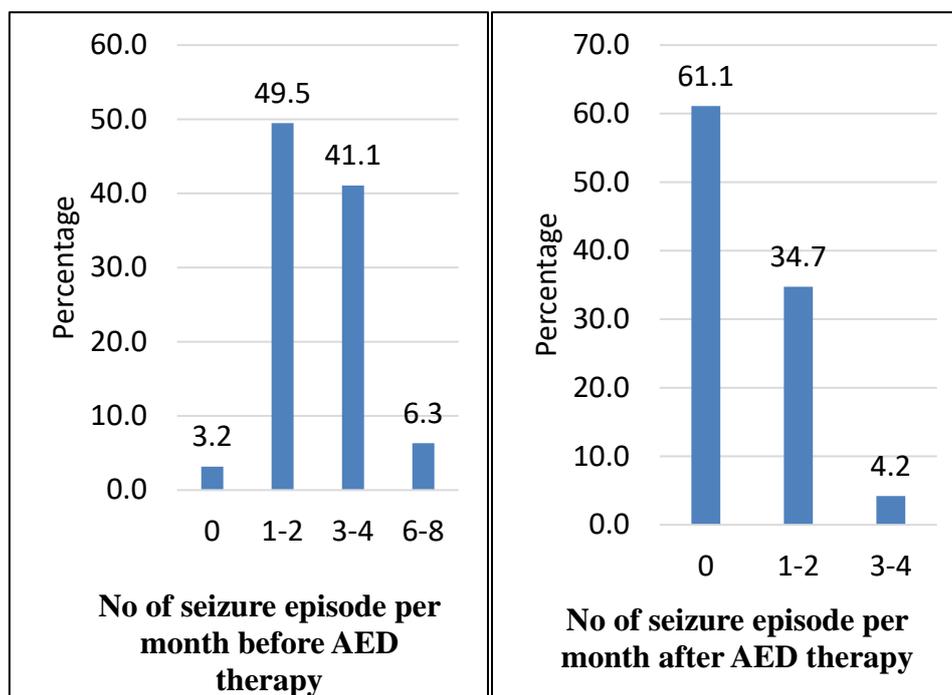


Figure 4: No of seizure episode per month after and after antiepileptic drug therapy

Valproate was prescribed in dosage range of 5-60 mg/kg among which most commonly prescribed dose is 11-20mg/kg followed by 5-10mg/kg. Carbamazepine is the second most common prescribed AED with dosage range of 15 -45mg/kg with most commonly prescribed dose of carbamazepine is 15mg/kg.

Out of all the 95 patients followed up for effectiveness of AEDs, 58% patients were seizure free in all the patients prescribed with valproate. Among them 94% patients were seizure free at 5-10mg/kg dosage and 73% patients were seizure free with carbamazepine from which 89% were having 15mg/kg dose. Levetiracetam made 20% patients' seizure free.

Discussion

The present study included only pediatric patients with confirmed diagnosis of epilepsy prescribed at least one drug. The present study maximum number (75.5%) of patient belong to less than 5 years of

age group which is in consonance with study carried out by Kousalya K. et al where majority of patient fall in 0 to 3 years category [11]. The study results of Mistry et al. and Trivedi and Dave are different from our study, where majority of patients fall in 6 to 10 years category [3,12].

In our study 62.1% patients were male whereas 37.8 patients were female with 1.6:1 of male to female ration. the results of gender distribution are similar to study carried out by Trivedi and Dave in 2018 where 63% patients were male and 37% were female [3]. This is also similar to study carried out in Gujarat by Mistry et al in 2014 where 69.8% were male and (30.2%) were female [12].

In educational status, 239 patients (around 40%) were attending school regularly. Repeated seizures discourage parents to enroll children to school and may also lead to irregularity in education. Seizures are known to affect personality and may affect

the study. In the study done in Gujarat by Mistry et al., 71.8% patients were attending school regularly.

American academy of neurology guideline for epilepsy recommended EEG as a part of routine neuro diagnostic evaluation for diagnosis and types of epilepsy though neither normal nor abnormal EEG alone excludes or confirms the diagnosis of epilepsy, also suggests diagnostic use of CT and MRI [13]. In the present study EEG was done in 102(17%) patients. MRI was done in 23 (3.8%) patients. This may be due to majority of the patients were from lower socio-economic class. Similar kind of results are observed by study conducted by Mistry et al [12].

The International League against Epilepsy classification of epilepsy and epileptic syndromes defines diagnosis and management of epilepsy. In the present study, majority of patients were having generalized epilepsy. Total number of patients having generalized epilepsy were 277 (46.2%), focal epilepsy was 151 (25.2%), remote symptomatic epilepsy was 58(9.68%), myoclonic Seizures were 8 (1.3%) and absence seizure were 7 (1.17%). In study done in Oman, generalized seizure was observed in the majority of cases in pediatric patients [14]. Other studies conducted at Malaysia showed that focal seizures are a major type of seizure [2].

The present study observed that valproic acid, carbamazepine, levetiracetam and Phenobarbitone account for more than 90% of total ASD prescribed. These are the majorly prescribed anti-epileptics similar to study done by Mistry et al. and Meenakshi et al. [12,15]. Other study by Bhatt et al. reported sodium valproate (25.11%) followed by phenytoin (11.41%) higher most prescribed drugs with 16% of newer antiepileptic drugs prescriptions [16]. As per practice guideline updates published in 2021 sodium valproate and

carbamazepine are the primary drugs in any epilepsy and levetiracetam is indicated

for add on ASD [17]. Among utilization pattern of other drugs, antipyretic group of the drug was most commonly prescribed [12]. Average number of drugs prescribed to every patient was 1.21 which was comparable to average number of drugs prescribed in study done by Meenakshi et al. [15]. Moreover, all the drugs were prescribed by generic names.

In the present study the most common drug prescribed to generalized seizure patient was valproate, to patients with focal epilepsy most common drugs prescribed was carbamazepine. Majority of myoclonic epilepsy patients were given valproate and clobazam combination. Most of the absence seizure patients were given sodium valproate. These results are similar to study done by Dave and Trivedi in 2018 [3].

The results of our study found that out of 599 patients, 61.1% patients were seizure free while 34.7% patients had 1-2 episodes per month and 4.2% patients were having 3-4 episodes of seizure per month after 6 months of continuous AED therapy. In majority of patients significant decrease in number of seizure episode was observed after initiation of AEDs. These were similar to study done by Dave and Trivedi where after AED therapy, seizure free patients were 63% and 35% patients had 3-4 episodes per month and 2% patients had 3-4 episodes per month [3].

The study does not report high rate of newer AEDs prescription. This might be due to the fact that clinicians are more conservative when treating younger children with newer AEDs compared to the adolescents; hence, the increase of newer AED prescribing is less significant when only investigating the younger age group of paediatrics [18]. LEV was most commonly used among newer AEDs, whereas a study in Italy showed gabapentin as the most commonly used newer AED [19].

Conclusion

The study has shown the patterns of different types of epilepsy prevalent in pediatric patients, drugs used among them along with useful baseline data and effectiveness of antiepileptic drugs. In the present study, GTCS was the most commonly observed type of seizure and sodium valproate was the most frequently prescribed drug to them followed by focal seizure. Most common drug prescribed to patients with focal seizure is Carbamazepine. Majority of patients were given monotherapy to achieve seizure control. Reduction in seizure episodes was noted with all the drugs and doses but highest seizure free patients were observed with lowest doses of AEDs. The higher doses were found less effective reason for which needs to be explored.

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