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Original Research Article

Drug utilization pattern of antiepileptic agents among pediatric epilepsy at tertiary care teaching hospital of Gujarat: a cross sectional study

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ABSTRACT

Background: Epilepsy is one of the most common neurological disorders characterized by recurrent episodic paroxysmal involuntary clinical events associated with abnormal electrical activity from the neurons. Without the knowledge of how drugs are being prescribed and used, it is difficult to initiate discussion on rationale drug use and to suggest measures to change prescribing habits for the better management. Present study was performed with an aim to study the utilization pattern of anti-epileptic drugs (AEDs) for the paediatric patients suffering from various forms of epileptic seizures.
Methods: The present cross-sectional study was conducted at the epilepsy clinic of Department of Paediatrics, Tertiary Care Teaching Hospital of Gujarat, on patients diagnosed to have epilepsy July 2014 to October 2014. Hundred Paediatric patients of either gender diagnosed to had epilepsy and taking treatment from pediatric epilepsy clinic OPD, S.S.G. Hospital, and Baroda. Patient's detailed medical history, demographic details and other required information was recorded on a prestructured data entry form.
Results: Out of 100. GTCS was found to be the most common (55%) form of epilepsy among pediatric patients and Carbamazepine was the most commonly prescribed (41%) AED followed by sodium valproate (38%). 71% patients were prescribed monotherapy. Carbamazepine +Clobazam was the most commonly (7%) used combination.
Conclusions: Use of appropriate AEDs in the majority of patients as per WHO guidelines, has decreased number of ADRs in this study.

Keywords: Carbamazepine, Cross-sectional study, Epilepsy, Seizures

INTRODUCTION

Drug Utilization Research is defined by WHO in 1977 as "The marketing, distribution, prescription and use of drugs in a society, with special emphasis on the resulting medical, social and economic consequences."[1] The principle aim of the drug utilization research is to facilitate rationale use of drugs in populations. For the individual patients, rationale use of a drug implies the prescription of a well-documented drug in an optimal dose for a right indication, with the correct information and at an affordable price.[1]

Without the knowledge of how drugs are being prescribed and used, it is difficult to initiate discussion on rationale drug use and to suggest measures to change prescribing habits for the better management. Information on the past performance of prescribers is the linchpin of any auditing system.[1]

Drug utilization studies are powerful exploratory tools to ascertain the role of drugs in society.[2] they create a sound sociomedical and health economic basis for health care decision making.[3] It is one of the most effective methods to assess the prescribing pattern of physicians.[4] Drug utilization studies play a pivotal role in directing towards

rational drug prescribing, thus minimizing the possibilities of adverse effects and helping improvement of patient compliance and resultant quality of life.

Epilepsy is one of the most common neurological disorders characterized by recurrent episodic paroxysmal involuntary clinical events associated with abnormal electrical activity from the neurons.[5]

The term *seizure* refers to a transient alteration of behaviour due to the disordered, synchronous and rhythmic firing of populations of brain neurons. Seizures can be "non-epileptic" when evoked in a normal brain by treatments such as electroshock or chemical convulsant or "epileptic" when occurring without evident provocation.[6]

Epilepsy affects about 20-40 million people worldwide.[7] It is the second most common neurological disorder, after stroke.[8] The rates are similar between different ethnic groups and slightly higher for men compared to women. Higher rates are reported in underdeveloped countries and lower socioeconomic classes. Across age groups, there is a bimodal distribution with higher incidence at extremes of age.[9]

Epilepsy is the most common neurological disorder in children with an incidence of about 8 per 1000 children under the age of seven years.[8] This childhood epilepsy remains a challenge to treat. Despite the increase in the number of Antiepileptic Drugs (AEDs), more than 25% of children with childhood epilepsy continue to have seizures. Around 4-10% of children suffer at least one seizure in the first 16 years of life. The incidence is highest in children below 3 years of age, with a decreasing frequency in older children. Epidemiological studies reveal that approximately 150,000 children will sustain a first-time unprovoked seizure every year, and of those, 30,000 will develop epilepsy.[10]

A large number of drugs are currently available for the treatment of epilepsy. Older/conventional drugs like Phenytoin, Carbamazepine, Valproic acid 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 are the newer ones and currently used as add-on or alternative therapy.

Despite of such heavy burden of diseases in paediatric age group, the current AED development system essentially renders children with epilepsy "therapeutic orphans" who can only benefit if the drugs developed for adults are also effective for children. The newer antiepileptic drugs are also being marketed for paediatric use in India as well as all over the world. However, there is lack of systematic pharmacoepidemiological studies investigating safety and efficacy of these AEDs in paediatric population. Antiepileptic treatment in paediatric age group should be aimed to control seizures associated with the lowest possible occurrence of adverse effects, thus allowing the

child to become an active member of the community and that too at the lowest possible overall cost.

Amongst the various factors affecting anti-epileptic drug (AED) usage, the major determinants are types of epilepsy, age and gender of patient, ease of dosing, efficacy, long term side effect profile, neuropsychiatric profile, sedative burden and interaction with other medications, co-morbid conditions medicines, affordability of the patient and preference of the treating physician as well as the practice setting. Present study was performed with an aim to study the utilization pattern of anti-epileptic drugs (AEDs) for the paediatric patients suffering from various forms of epileptic seizures.

METHODS

The present cross-sectional study was conducted at the epilepsy clinic of Department of Paediatrics, Tertiary Care Teaching Hospital of Gujarat, on patients diagnosed to have epilepsy July 2014 to October 2014. Hundred Paediatric patients of either gender diagnosed to had epilepsy and taking treatment from pediatric epilepsy clinic OPD, Tertiary Care Teaching Hospital of Gujarat. Based on a previous record, on an average 14-15 paediatric patients came to epilepsy clinic per week. Amongst them 5-6 were new patients while remaining came for follow-up. On this basis of estimated sample size of patients who had received at least 2 months antiepileptic drug therapy was calculated as 100.

Inclusion criteria

Patients of both gender and age less than 18 years, diagnosed to have epilepsy, and receiving drug therapy for at least 2 months were included in this study.

Exclusion criteria

Patients with secondary epilepsy due to head injury, cerebral palsy, stroke, metabolic disorders etc, Patients not willing to participate in the study were excluded from our study.

Patients fulfilling the inclusion and exclusion criteria were included in the study. Patient / Legally Authorized Representative (LAR) were informed about the nature of study. Written informed consent was obtained from parent and ascent was obtained from child whenever applicable and only those patients from whom informed consent was obtained were enrolled in the study. Patient's detailed medical history, drug reports, demographic data, type of seizures, the anti-epileptic drugs prescribed and the adverse drug reactions (ADRs) reported by the patients were recorded in a prestructured data entry form.

Statistical analysis

The data was coded and entered into Microsoft Excel spreadsheet. Analysis was done using SPSS version 15

(SPSS Inc. Chicago, IL, USA) Windows software program. The variables were assessed for normality using the Kolmogorov-Smirnov test. Descriptive statistics were calculated. Paired t test was used to evaluate the effectiveness of AED therapy

RESULTS

Total 100 pediatric patients of either gender diagnosed to had epilepsy and who had received at least 2 months antiepileptic drug therapy from pediatric epilepsy clinic OPD, Tertiary Care Teaching Hospital of Gujarat during July 2014 to October 2014 were recruited in the study.

As shown in Table 1, among 100 patients recruited, 40 patients each belonged to 5-10 and 10-15 year age group while 17 patients were from 0-5 year age group and remaining 3 patients were from 15-18 year age group, at the time of admission. Out of 100 patients, 63 were males; while 37 were females (Table 2).

Table 1: Age wise distribution.

Age	No of patients
0-5 year (Age)	17
5-10 year (Age)	40
10-15 year (Age)	40
15-18 year (Age)	3
Total No of Patients	100

Out of 100, almost half (47%) of sample population had family income <50000 INR annually while 34% had

annual family income of 50000-100000 INR. Out of 100 patients 72 patients were school going and 28 patients had never gone school. Out of 100 patients 87 patients were immunized and remaining 13 patients were partial / non immunized.

Table 2: Gender wise distribution.

Gender	Total no of patients (100)
Male	63
Female	37
Total	100

Out of 100 patients 79 Patients were underweight, 20 were classified into normal weight category while only 1 child was overweight (obese class - 1). Out of 100 patients 91 patients had no family history of epilepsy while remaining 9 patients had family history of epilepsy.

Out of 100 patients EEG alone was used as a diagnostic test in 49 patients and EEG and CT SCAN were used as a diagnostic test in 35 patients. EEG and MRI were used as diagnostic tests in 9 patients and in remaining 7 patients EEG, MRI, and CT SCAN all were used as diagnostic tests. Out of 100 patients 55% patients had generalized tonic clonic seizure while 18 and 19% patients had Partial seizure and focal seizure respectively. Myoclonic seizure and benign rolandic seizure were seen in 5 and 2 patients respectively. Only 1 patient suffered from absence seizure (Table 3).

Table 3: Distribution of patients according to type of seizure.

GTCS	Focal seizure	Partial seizure	Myoclonic seizure	Benign rolandic epilepsy	Absence seizure	Total no of patients
55	19	18	5	2	1	100

Out of 55 patients who suffered from generalized tonic clonic seizure 42 patients were prescribed monotherapy, 8 patients were prescribed double drug regimen, 5 patients were prescribed triple drug regimens. Out of 19 patients who suffered from generalized focal 11 patients were prescribed monotherapy, 6 patients were prescribed double drug regimen, 2 patients were prescribed triple drug regimens. Out of 18 patients who suffered from Complex Partial Seizure 14 patients were prescribed monotherapy, 4 patients were prescribed double drug regimen. Out of 5 patients who suffered from Myoclonic seizure only 1 patient was prescribed Carbamazepine as a monotherapy. Double drug regimen was prescribed to 3 patients. Which were valproate + clonazapam, valproate + levetiracetam, levetiracetam + phenobarbitone. Triple drug regimen was prescribed to one patient which was sodium valproate + levetiracetam + lamotrigine.

Table 4: Total no of AEDS prescribed in each seizure.

GTCS	Focal seizure
74	30
(54%)	(22%)
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74	30
(54%)	(22%)
GTCS	Focal Seizure
74	30
(54%)	(22%)
GTCS	Focal Seizure

As per the Table 4 and Table 5, total no of 138 drugs were prescribed in 100 pediatric epilepsy patients. Out of which 74 (54%) AEDs were prescribed to the patients of general

tonic clonic seizure and 30 (22%) AEDs were prescribed to the patients of focal seizure followed by 21 (15%) were prescribed to the patients of complex partial seizure and 10 (7%) AEDs were prescribed to the patients of Myoclonic seizure and in the patients of absence seizure and benign rolandic epilepsy respectively 1 (1%) and 2 (1%) drugs were prescribed. Out of Total 138 drugs prescribed, carbamazepine was the most commonly prescribed drug (41%) followed by sodium valproate (38%) and clobazam (9%).

Total 21 drugs were prescribed to 18 patients who were suffering from complex partial seizure. Out of which carbamazepine was the most frequently prescribed drug (66.66%) followed by valproate (23.80%) and clobazam (9.52%). Total 10 drugs were prescribed to 5 patients who were suffering from myoclonic seizure. Out of which sodium valproate (30 %) and levetiracetam (30 %) were

the most frequently prescribed drugs respectively. In this study we found that total 2 drugs prescribed in 2 patients who were suffering from benign rolandic seizure. Both drugs are carbamazepine. One patient who suffered from absence seizure was prescribed sodium valproate (Table 6).

Table 5: Total no of AEDS prescribed.

Drug	No of drugs prescribed
Carbamazepine	56 (41%)
Sodium Valproate	53 (38%)
Clobazam	12 (9%)
Levetiracetam	9 (6%)
Clonazepam	4 (3%)
Phenobarbitone	3 (2%)
Lamotrigine	1 (1%)
Total no of drugs	138

Table 6: No of AED prescribed in each seizure.

Drugs	GTCS	Focal seizure	CPS	Absence seizure	Myoclonic seizure	Benign rolandic epilepsy	Total no of drugs	Drugs	GTCS
Carbamazepine (56)	22	17	14	0	1	2	56	Carbamazepine (56)	22
Sodium valproate (53)	38	6	5	1	3	0	53	Sodium Valproate (53)	38
Clobazam (12)	5	5	2	0	0	0	12	Clobazam (12)	5
Levetiracetam (9)	5	1	0	0	3	0	9	Levetiracetam (9)	5
Clonazepam (4)	2	1	0	0	1	0	4	Clonazepam (4)	2
Phenobarbitone (3)	2	0	0	0	1	0	3	Phenobarbitone (3)	2
Lamotrigine (1)	0	0	0	0	1	0	1	Lamotrigine (1)	0
Total	74	30	21	1	10	2	100	Total	74

Table 7: No of seizure episode per month before antiepileptic drug therapy.

1-2 episodes of seizure per month	3-5 episodes of seizure per month	6-8 episodes of seizure per month	>8 episodes of seizure per month	Total no. of patients
41	53	4	2	100

Out of 100 patients, 63 patients were seizure free while 35 patients had 1-2 episodes per month after starting AED therapy. 2 patients were having 3-4 episodes of seizure per month after AED therapy. In majority of patients

significant decrease in no. of seizure episode ($P<0.0001$) was observed after starting AED (Table 7).

Table 8: No of seizure episode per month after antiepileptic drug therapy.

Seizure free patients	1-2 episodes of seizure per month	3-4 episodes of seizure per month	Total no. of patients
63	35	2	100

DISCUSSION

Epilepsy is the most common neurological disorder in children characterized by spontaneous propensity for

recurrent and unprovoked seizures and it remains a Challenge to treat.[11,12] Despite of overall increase in number of antiepileptic drugs, more than 25% of children with childhood epilepsy continue to have seizures.[12]

The overall aim of antiepileptic treatment should be to control seizures with the lowest possible occurrence of adverse effects, allowing the child to become an active member of the community and this at the lowest possible overall cost. This Outdoor Patient Department (OPD) based cross-sectional study aims at providing a snapshot of the AED usage pattern in this tertiary care hospital.

In this study, majority of the patients (40%) belonged to age group 6 to10 years with a Mean age of patient was found to be 9.14±3.65 years. This is in consonance with the study carried out in Malaysia.[13] and it is in contrast to the some other study in which majority of children fall in 0 to 3 year age group.[14]

In the present study, out of total, 86% patients were immunized, which is almost similar to study carried out by Mistry et al.[15] Certain diseases like measles, diphtheria, pertussis, tetanus etc., cause brain damage as well as febrile episodes which may result in to febrile convulsions. So immunization plays an important role in prevention of epilepsy.[16]

Majorities of the patients (72 %) included in this study were going to school. Due to frequent seizure episodes, maintenance of regular activity may become difficult for the patients who may result in to school dropout or irregularity in school.

In this study, EEG was used in all 100 patients for diagnosis of epilepsy which was higher as compared to previous study conducted by Mistry et al.[15] EEG alone was used as an investigation of epilepsy in 49% patients. As per American academy of neurology guideline for epilepsy, EEG plays only a part of routine neurodiagnostic evaluation for diagnosis of epilepsy and on the basics of normal and abnormal EEG alone, we can't confirm the diagnosis of epilepsy.[16] In this study we found that MRI and CT Scan was done in only 16% and 42% patients respectively.

The probable reason, why the investigations were not carried out as per American academy of neurology guidelines is, as majority of the patients belonged to lower socioeconomic class and almost 81% patient's family had their annual income below 100000 INR/Year, they may not afford the cost of CT Scan and MRI.

Generalized tonic clonic seizure was the most commonly observed seizure in the present study. Percentage of patients suffering from generalized tonic clonic seizure was higher than that observed by other studies.[16,17] The most commonly prescribed drug in the present study was carbamazepine followed by sodium valproate which is similar to study conducted by Mistry et al, and in contrast to study conducted by Kousalya K et al, which reports that sodium valproate was the commonest drug used for seizure, followed by phenytoin.[14,15]

In this study we found that the most commonly prescribed drug in GTCS was Sodium valproate which was similar to studies conducted by Mistry et al, and Kousalya K et al.[14,15] While most commonly prescribed drug in Focal Seizure was Carbamazepine which was similar to studies conducted by Mistry et al, and in contrast to study conducted by Kousalya K et al, which reports that phenytoin was the commonest drug used for focal seizure.[14,15]

As per the guidelines of treatment of epilepsy sodium valproate and Carbamazepine are recommended for GTCS Patients and focal seizure patients respectively.[18,19] in this study we found that most commonly prescribed newer drug was clobazam this is in consonance with study carried out by Mistry et al.[15]

Single AED (monotherapy) was prescribed to 73.5% patients. Findings of our study are in consonance with findings of the other studies.[14,15] Moreover, majority (80.43%) of the drugs were prescribed by generic name.

As the present study was done in a tertiary care teaching government hospital, complete data regarding the types of AEDs prescribed in various forms of paediatric epilepsy and economical burden of the same could not be evaluated and the sample size of study population was less due to time constrain.

CONCLUSION

In the present study, GTCS was the most commonly observed type of seizure and Carbamazepine was the most frequently prescribed drug followed by sodium valproate. Most frequently observed seizure was drowsiness followed by irritability in majority of cases, AEDs were prescribed as per WHO standard treatment guidelines.

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