Anti-Convulsant Drugs Prescribing Pattern and Efficacy Comparison in Paediatric Epilepsy Population in a Tertiary Care Teaching Hospital

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ABSTRACT

Objectives: To conduct the study of the drug usage pattern and its efficacy and tolerability comparison of most commonly used anti-epileptic drugs. Methods: The data included patient’s age, sex, types of seizure, aetiology, past and present treatments, dose and duration of therapy and associated adverse effects. A total of 150 subjects (children) who received Sodium valproate (n = 88), Carbamazepine (n = 21), Phenytoin (n = 7), Clobazam (n = 11), Levetiracetam (n = 4) and remaining in combinations (n = 19) as long-term management, were enrolled in the study. Assessed for a period of 12 months for the management of seizures and also the adverse effects incidents.

Results: Total, 91 (60.7) subjects endured from seizure episodes throughout the study interval of 12 months. 131 (87.3%) patients were treated with Monotherapy, the rate of seizure remission was 81 (61.8%) and 19 (12.6%) patients were with multidrug therapy, the rate of seizure remission was 11 (57.8%). The rate of seizure remission was found statistically significant. 60 patients treated with Sodium Valproate, 19 patients treated with Carbamazepine, 1 patient treated with Phenytoin, 9 patients with Clobazam, 2 patients treated with Levetiracetam were observed to be seizure free. The most commonly occurred type of seizures was GTCS and Focal/Partial type. Overall, 67 (44.6%) patients had adverse effects; of the highest incidence was cognitive impairment, mood alterations and dizziness which developed more often with Sodium Valproate and Carbamazepine. Conclusion: In our collected and observed study in tertiary care teaching hospital the majority of patients were prescribed with Sodium Valproate and Carbamazepine. It appears that Sodium Valproate and Carbamazepine has highest efficacy rate and Levetiracetam had better tolerability. Sodium valproate and Carbamazepine had balanced effectiveness and tolerability.

Key words: Anti-epileptic drugs, Efficacy, Tolerability, Monotherapy, Polytherapy, reoccurrence.

INTRODUCTION

A chronic neurological disorder specified with repeated unprovoked seizures is called as epilepsy.¹-⁴ Recurrent, episodic, involuntary, clinical events associated with abnormal electrical activity from the neurons are the characteristic features. Abnormal excessive hypersynchronous electrical impulses produces single or paroxysmal events from the brain that is central nervous system resulting in abnormal involuntary, motor, sensory, autonomic or sensorial activity.⁵ Epileptic seizures commonly cause transitory loss of consciousness parting the single at risk of bodily harm and usually interferes with education and employment.⁶ Epilepsy affects about 70 million people worldwide. Nearly 90% of those suffering from epilepsy are in developing regions.⁷ In India the prevalence level of epilepsy sorts between 4.15 and 7.03 per 1000 population.⁸ In 2017, universally assessed that each year near and around 2.4 million people are identified with epilepsy. About 14 people per 1000 populations are disposed to suffer from epilepsy in India with upper evaluations in children, young adults and in rural areas.⁹ In 2018 the occurrence of epilepsy was found 0.3-0.5 percent among varied populations all over the world. In India the frequency is 5-10 persons per 1000 at a predictable rate.
Nearly 80% people suffer from epilepsy were in low and middle income countries.\(^{10}\)

Compliance with medications has become a foremost problems because of the prolonged treatment associated with undesirable effects of many drugs.\(^{11}\) Prevention of seizures and avoidance of adverse events with the regimen that is suitable and easy to follow is the primary goal of antiepileptic therapy. Antiepileptic drug of choice depends on type of seizures and patients age.\(^{12}\)

The study focus is to analyse the antiepileptic medication safety, effectiveness and tolerability in paediatric department at MGM Hospital located in Warangal, Telangana, India.

**MATERIALS AND METHODS**

**Methods**

The study is a prospective, observational and comparative. It is performed in Paediatrics department at Mahatma Gandhi Memorial Hospital Warangal, Telangana, India. MGM hospital is a 1000-beded tertiary care hospital facilitated with advanced diagnostics and therapy. Patients from various regions includes Telangana and Andhra Pradesh visited the hospital belonged to diverse socioeconomic divisions. The study was done for a period of 12 months.

**Consent**

The study protocol was submitted to Institutional Human Ethics committee and got approved. The IHEC number was MGMH/VCOP/PHARM D/V/015/2017. All the patients were explained about the process of work in their language and procured informed consent from them.

**Inclusion criteria**

1. The study included subjects of paediatric population who were diagnosed with epilepsy.
2. Patients of both genders (male and female).
3. Patients who are interested to participate are considered and given informed written consent.

**Exclusion criteria**

1. Patients with other genetic or medical disorder.
2. Adults are excluded.
3. Patients of age above 14 years are not considered in study.
4. Newly diagnosed patients are excluded.

**Statistical Analysis**

Baseline data of demography, aetiology, types, severity and frequency of seizures, efficacy and anti-epileptics were calculated using Statistical package for social sciences software, version 20. The obtained data was statistically evaluated using one-way analysis of variance (ANOVA). Significance was identified between two dependent variables using spearman rank correlation and found statistically significant result that is a two-tailed P-value less than 0.05.

**RESULTS**

**Socio-demographic details of patients**

Table 1 shows the study included a paediatric population of 150 subjects for the study period of 12 months in which incidence of female were 62 (41%) and males were 88 (59%). The AED’s were prescribed highly to the age group of 7-12 years (50%) then 1-6 years (40%).

**Seizure aetiology, types and frequency of seizures**

Table 2 reveals the seizure aetiology in the present study was found to be the most with febrile condition 43(28.7%), idiopathic seizures 35(23.3%), family history 29(19.3%), head injury 23(15.3%). We found scanning reports (EEG, CT-Scan, MRI Scan) for 102 patients in that 63 patients were found with normal condition and 15 patients from abnormal to normal condition after long-term treatment with anti-epileptics. The reoccurrence of seizures was high in age group of 1-6 years there was a statistically significant correlation. GTCS type 64 (42.7%) and focal/partial type 21 (14%) of seizures were the most commonly occurred type of seizures in the collected and observed study.

**Tolerability**

Table 3 shows the tolerability, was assessed by incidence of adverse effects of drugs while on long term treatment. The most frequently occurred adverse effects were mood alterations and cognitive impairment, which developed more often with sodium valproate and Carbamazepine. Dizziness was frequently occurred with sodium valproate and Clobazam. Anger that is behavioural problems was most occurred with sodium valproate.

**Anti-epileptic drugs prescribed among different types of seizure patients in the collected subjects**

Figure 1 and 2 shows Sodium valproate 88(58.7%) then Carbamazepine 21 (14%) were the commonly prescribed
drugs. Overall antiepileptic drugs usage as monotherapy and polytherapy.

**Efficacy in Monotherapy**

Figure 3 reveals the reoccurrence rate was as follows: sodium valproate 25.90%, Carbamazepine 10%, Levetiracetam 50%, phenytoin 71.40%, Clobazam 85%. The data was represented in Figure 3. The lowest reoccurrence rate was with carbamazepine and then sodium valproate. So, these were observed to be most efficacious.

**Efficacy in combinational therapy**

Figure 4 shows the Sodium valproate and Carbamazepine combination was found to be better efficacious with lowest reoccurrence rate of 12.5%.

**DISCUSSION**

Many factors persuade treatment collection include age, sex, types of seizures, aetiology, simultaneous antiepileptics. Successful therapy ought to obtain balance in procuring remission or control of seizure episodes and side effects. Present study demonstrates that Carbamazepine and Sodium valproate were most frequently prescribed monotherapy drugs. Childhood epilepsy had a generally favourable outcome, with 90% no reoccurrence rate with Carbamazepine and 74.1% with Sodium valproate which shows better efficacy in seizure control. The AED’s Sodium valproate, Carbamazepine, Clobazam, Levetiracetam and Phenytoin were compared with monotherapy and their combinations. It was observed that 131 (87.3%) patients were treated with monotherapy, the rate of seizure remission rate was 81 (61.8%) and 19 (12.6%) patients were with multidrug therapy, the rate of seizure remission was 11 (57.8%).

**Efficacy**

In previous study, Unsal et al. 2014 had shown that 83.7% where the rate was significantly higher for seizure-free with Valproate Monotherapy in children. They observed total remission rate of 84.8% for twelve months which shows similar or slightly higher than several other studies where the control rate of seizures was between 50% and 84% for first line anti-seizure drug treatment in children. Our study in paediatrics, 131 (87.3%) were on
monotherapy in that 81 (61.8%) seizure control rate was observed, which was significant.

**Antiepileptic drug efficacy comparison in our study**

In our analysis, the majority given antiepileptic drugs were Sodium valproate and Carbamazepine. The potency was not similar in all drugs which were taken in our study. Unsal et al. 2014 had shown related beneficial rates with all AEDs which includes Carbamazepine, Valproate, Oxcarbazepine, Phenobarbital and Levetiracetam. Based on their comparative study under conventional care with phenytoin, carbamazepine, valproate and phenobarbital had shown analogous result of benefits and adverse events. In our study, Sodium valproate, Carbamazepine, Clobazam, Levetiracetam, Phenytoin were compared with monotherapy and their combinations for efficacy and safety. The results were found to be, Carbamazepine and Sodium valproate had shown better efficacy with statistically significant.

In previous study Lage et al. 2005 reported that, among 90% of patients taking Levetiracetam mono therapy shown greater than 50% subjects with seizure depletion. The data availability on efficacy of carbamazepine and phenytoin in our study were limited. In the present study, Levetiracetam and Phenytoin doesn’t have better efficacy in monotherapy.

**Tolerability**

**Adverse effects:** In our study, the drugs carbamazepine, clobazam, levetiracetam, sodium valproate and phenytoin tolerability was assessed by using the highest incidence of adverse drug effects. The highest incidence of three major adverse effects was cognitive impairment, mood alterations and dizziness with sodium valproate and Carbamazepine. Even though there is highest incidence of adverse effects with sodium valproate and Carbamazepine the study was observed that these drugs had better tolerability. We found no significant difference in the efficacy and tolerability with these drugs. Monotherapy of Levetiracetam had shown no adverse effects in the present study.

Dudley et al. 2009, evaluated that therapy failed in terms of adverse effects and ineffectiveness put up parallel to anti-epileptic first line agents in children. Our study suggest, that adverse effects which occur with the most frequently prescribed drugs and better efficacious drugs are to be monitored cautiously and/or to avoid the risks of cognitive problems setting of low doses is to be followed.

**Table 1: Socio-demographic details.**

<table>
<thead>
<tr>
<th>Gender</th>
<th>No. of patients (n=150)</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>88</td>
<td>59%</td>
</tr>
<tr>
<td>Female</td>
<td>62</td>
<td>41%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age</th>
<th>No. of patients (n=150)</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-12 months</td>
<td>3</td>
<td>2%</td>
</tr>
<tr>
<td>1-6 years</td>
<td>60</td>
<td>40%</td>
</tr>
<tr>
<td>7-12 years</td>
<td>75</td>
<td>50%</td>
</tr>
<tr>
<td>13-14 years</td>
<td>12</td>
<td></td>
</tr>
</tbody>
</table>

**Table 2: Types of seizures and their frequencies.**

<table>
<thead>
<tr>
<th>Types of seizures</th>
<th>Frequency (150)</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>GTCS</td>
<td>67</td>
<td>44.6%</td>
</tr>
<tr>
<td>Focal seizures</td>
<td>23</td>
<td>15.3%</td>
</tr>
<tr>
<td>Complex partial seizures</td>
<td>10</td>
<td>6.6%</td>
</tr>
<tr>
<td>Simple partial seizures</td>
<td>6</td>
<td>4.0%</td>
</tr>
<tr>
<td>Complex febrile seizures</td>
<td>5</td>
<td>3.3%</td>
</tr>
<tr>
<td>Simple febrile seizures</td>
<td>5</td>
<td>3.3%</td>
</tr>
<tr>
<td>Absence seizures</td>
<td>5</td>
<td>3.3%</td>
</tr>
<tr>
<td>Atonic seizures</td>
<td>2</td>
<td>1.3%</td>
</tr>
<tr>
<td>Status epilepticus</td>
<td>14</td>
<td>9.3%</td>
</tr>
<tr>
<td>Tonic seizures</td>
<td>8</td>
<td>5.3%</td>
</tr>
<tr>
<td>Unprovoked seizures</td>
<td>3</td>
<td>2%</td>
</tr>
<tr>
<td>Provoked seizures</td>
<td>2</td>
<td>1.3%</td>
</tr>
</tbody>
</table>

**Table 3: Tolerability of drugs.**

<table>
<thead>
<tr>
<th>Adverse effects</th>
<th>Sodium valproate</th>
<th>Clobazam</th>
<th>Carbamazepine</th>
<th>Phenytoin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cognitive impairment</td>
<td>28.55</td>
<td>7.1</td>
<td>35</td>
<td>0</td>
</tr>
<tr>
<td>Mood alterations</td>
<td>22</td>
<td>7.1</td>
<td>30</td>
<td>14.2</td>
</tr>
<tr>
<td>Dizziness</td>
<td>10.3</td>
<td>14.2</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Anger</td>
<td>7.7</td>
<td>0</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Dullness</td>
<td>3.8</td>
<td>7.1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Weight gain</td>
<td>1.2</td>
<td>0</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Rashes</td>
<td>2.5</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Hypotension</td>
<td>1.2</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
CONCLUSION

In conclusion, our study observed that the majority of patients were prescribed with sodium valproate and Carbamazepine. Based on seizure free and seizure control rate sodium valproate and Carbamazepine were considered as better efficacious drugs. Levetiracetam had better tolerability. Even though there was highest incidence of adverse effects, i.e., cognitive impairment, mood alterations and dizziness with sodium valproate and Carbamazepine the study were observed that these drugs had better tolerability. Our study suggests that drugs which had highest efficacy also had highest incidence of adverse effects hence monitor cautiously.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest

ABBREVIATIONS

AEDs: Anti-Epileptic Drugs; ANOVA: Analysis of Variance; MRI: Magnetic Resonance, EEG: Electro encephalogram; CT scan: Computed tomography; GCTs: Generalized Tonic Clonic Seizures; VPA: Sodium Valproate; PHY: Phenytoin; CLO: Clobazam; LEV: Levetiracetam; CARB: Carbamazepine.

SUMMARY

The most commonly prescribed anti-epileptic medications were sodium valproate and carbamazepine and these two drugs shown highest efficacy rate in controlling episodes of seizure occurrence. Even though they show highest efficacy they had highest incidence of adverse effects hence monitor attentively.

REFERENCES