Original Article

Prescribing Pattern of Anti-epileptic Drugs and Measures to Overcome Ubiquitous Hurdles to Improve Quality of Life in Epileptic Patients

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ABSTRACT

Background: In our nation, several patterns of antiepileptic medication use have been documented. Newer medications are becoming accessible, and it will be fascinating to observe how they are used. Clinical pharmacists can identify and manage issues in antiepileptic therapy such as polytherapy, adverse drug responses, drug interactions, and medication non-adherence. **Methods:** All in-patients in the Paediatric and General Medicine department who were prescribed anti-epileptic medicines were considered. After obtaining patient consent, data was gathered via a customized data collection form as well as from patient case sheets/prescriptions. Data have been calculated with descriptive statistics as a percentage and frequency. To summarize the data analysis, Microsoft excel was used. **Results:** Out of 60 patients, 65% were males and 35% were females. The Male: Female ratio was 1.85:1. The mean age was 47.15 + 19.05 yrs. Tonic-clonic seizures were diagnosed in around 50% of the cases, Unknown seizures in 25% of the cases, Partial onset in 7% of the cases, and Focal Onset, symptomatic in 5% of the cases each. Acute and pseudo seizures in 3% of the cases each. Syncope seizures in 2% of the cases. In Anti-epileptic drugs, Levetiracetam was the most commonly prescribed drug used in 50% of the cases. Antiepileptic drug interaction was seen in 19 cases around 32% of the cases. Antiepileptic drugs interaction was severe in 53% of the cases, Moderate interaction in 16% of the cases, and Mild interaction in 32% of the cases. **Conclusion:** Despite the use of a suitable Antiepileptic drugs, patients experienced an increase in the frequency of seizures as well as the occurrence of adverse effects. This issue may have been avoided by providing adequate dosage and avoiding polytherapy wherever feasible.

Keywords: Antiepileptics drug, Monotherapy, Drug interaction, Polytherapy.

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INTRODUCTION

Epilepsy is a prevalent neurological illness, including a diverse range of illnesses characterized by the recurrence of seizures. A seizure is a single (finite) occurrence of aberrant brain discharge, epilepsy is a chronic condition defined by abnormal recurrent seizures, and the epileptic syndrome is an epileptic illness defined by a cluster of signs and symptoms that usually occur simultaneously.[1] Epilepsy affects over 50 million individuals globally and accounts for a considerable amount of the global illness burden. This is most likely attributable to an increased risk of endemic diseases like malaria or neurocysticercosis; a higher incidence of road traffic accidents; birth-related injuries; and disparities in medical infrastructure, preventive health programs, and access to care. Nearly 80% of epilepsy patients are from lower and middle-income nations.[2] Epilepsy patients with frequent or persistent seizures generally have a poor quality of life. Epilepsy, in reality, imposes a significant financial burden on the patients and their families. The goal of epilepsy therapy is to achieve seizure-free conditions while minimizing side effects. However, the seizure-free condition is frequently exaggerated to the point of causing side effects.[3-4]

Antiepileptics are the cornerstone for the treatment of epilepsy. There are two main types of antiepileptics, the older and new generation. Phenytoin, Phenobarbital, Primidone, Ethosuximide, Benzodiazepines, Carbamazepine, and Valproates were older (traditional) Antiepileptic drugs while Felbamates, Gabapentin's, Lamotrigine and Pregabalin, etc are newer generation Antiepileptic drugs. Over the previous two decades, Numerous Antiepileptic drugs were launched onto the market. Many of these drugs are currently undocumented in terms of their safety, including their use in certain patient populations such as children, pregnant women, and the elderly.[5]

Antiepileptic drugs are used to treat peripheral neuropathy, migraines, essential tremor, stiffness, restless legs syndrome, bipolar disorder, schizophrenia, and anxiety disorders, among other non-epilepsy illnesses. These ailments are treated with both traditional and contemporary Antiepileptic drugs. TBI, Parkinson's or Alzheimer's disease, alcoholism, and obesity are all treated with antiepileptics.[6] Only a few anti-epileptic medications were available until recently, and they all had serious adverse effects. A number of novel Antiepileptic drugs have been developed since 1990. Newer Antiepileptic drugs are often used as a complement to older Antiepileptic drugs in those who have epilepsy that cannot be controlled with them alone. Newer Antiepileptic drugs are touted as being just as effective as older ones, but with fewer adverse effects.[7] Regardless of the fact that there are over 20 antiepileptic drugs on the market, around 30% of people are resistant to treatment. A significant aspect of Pharmacoresistant epilepsy is that most patients with refractory epilepsy are resistant to numerous, if not all, Antiepileptic drugs, despite the fact that these drugs function through different routes. Pharmacoresistant epilepsy is a critical health problem that has been related to higher rates of morbidity and death, as well as a considerable financial burden on epileptic patients.[8-9]

In affluent countries, non-adherence to chronic illness treatment ranges from 30 to 50 %, whereas it is substantially higher in poor countries. It's quite fascinating because, after 2-5 years of treatment, 60% of treated persons cease taking their medication without relapsing. The patient's adherence behaviour can be improved in order to properly control epilepsy. Anti-epileptic drugs also have concerns with adverse drug reactions (ADRs) and drug interactions. These are crucial clinical issues in both paediatrics and adult medicine. The most latest Antiepileptic drugs have a multitude of side effects. Furthermore, the toxicity of medications in Antiepileptic drug clinical studies is under-reported.[10]

MATERIALS AND METHODS

Type of Study: Random cross-sectional, observational, single centred study.

Place of Study: Thumbay New Life Hospital.

Sample size: 60 patients

The study included 60 individuals who were prescribed Antiepileptic drugs for seizure disorders and presented to the hospital's Inpatient and outpatient departments or pediatric units.

The study's purpose and procedure were described to them, and participants gave written informed consent. The data obtained were recorded in a case record form, and the prescriptions were analyzed for details such as the patient's demographic profile (gender and age), condition profile/diagnosis, details of the drugs prescribed, and whether the drugs prescribed were in accordance with the WHO core prescribing indicators and if the therapy was in accordance with standard guidelines.

Drug information such as the drug's name, dosage type, dosing frequency, duration, method of administration, and diagnostic data was also recorded.

Anti-epileptic drugs being prescribed to all patients in the Pediatric and General Medicine departments. Patients with comprehensive medical records who are willing to participate in the research and have seizures were included in the study.

Pregnant and Lactating women and Patients with psychiatric problems were excluded from the study.

Ethical Clearance: Ethical clearance was obtained from the institutional ethics committee prior to the commencement of the study.

Statistical Analysis: Ms-Excel was used to calculate the data and patient-related parameters. The results were represented as a percentage/ proportion in the form of a bar diagram and a pie chart, as well as in tabular form. The mean was also displayed, and the data was shown to two significant decimal places.

OBSERVATION AND RESULTS

A total of 60 patients who met the inclusion criteria were included in this study. Out of 60 seizure patients, 65% were males and 35% were females. The Male: Female ratio was 1.85:1. The majority of the patients around 25% belonged to the age group of 51 to 60 yrs followed by 22% in the 41 to 50 years age group. The least belonged to the age group of 61 to 70 yrs with 8%. The mean age was 47.15 + 19.05 yrs.

Out of 60 patients, 37% of the patients were or had used medication previously for seizures. 27% of the patients consumed alcohol and few had alcohol withdrawal symptoms leading to seizures. Nearly 23% of the cases were smokers. Nicotine which is found in tobacco increases the risk of seizures.

62% of the patients had high BP and 23% had high pulse rate which is a risk factor for seizures. SPO2 was <95% in around 3% of the cases.

Tonic-clonic seizures were diagnosed in around 50% of the cases, Unknown seizures in 25% of the cases, Partial onset in 7% of the cases, and Focal Onset, symptomatic in 5% of the cases each. Acute and pseudo seizures in 3% of the cases each. Syncope seizures in 2% of the cases.

In Anti-epileptic drugs, Levetiracetam was the most commonly prescribed drug used in 50% of the cases. Phenytoin was the next most prescribed drug in 15% of the cases. Lacosamide was prescribed in 12% followed by Lorazepam in 11% of the cases. Clobazam was prescribed in 5% of the cases. Midazolam and Valproic acid were prescribed in 3% of the cases each. The least prescribed drug was Diazepam in 1% of the cases.

Table 2: Types of anti-epileptic drugs prescribed.

Drugs	Frequency (N)	Percentage (%)
Phenytoin	15	15.00%
Lorazepam	11	11.00%
Clobazam	5	5.00%
Levetiracetam	50	50.00%
Midazolam	3	3.00%
Valproic acid	3	3.00%
Lacosamide	12	12.00%
Diazepam	1	1.00%
Total	100	100%

Table 3: Distribution based on generation of antiepileptic drugs and Mono or polytherapy.

Type of antiepileptic drugs	Frequency(N)	Percentage (%)
1st Generation antiepileptic	37	37.00%
2nd Generation antiepileptic	51	51.00%
3rd Generation antiepileptic	12	12.00%
Number of antiepileptic drugs per prescription		
Monotherapy		
1	26	43.33%
Polytherapy	34	
2	15	44.11%
3	13	38.23%
4	6	17.64%
Total	60	100%

Table 4: Antiepileptic Drug Interactions and mechanism of drug interaction.

Type of drug interaction	Frequency (N)	Percentage (%)
Mild	6	31.57%
Moderate	3	15.78%
Severe	10	52.63%
Total	19	100%
Mechanism of drug interaction		
Pharmacokinetics drug interactions	12	63.15%
Pharmacodynamic drug interactions	5	26.31%
Both	2	22.22%
Total	19	100%

Table 5: Drug-drug interaction with Antiepileptic drugs.

Objective drug	Precipitated drug	Frequency (N)	Percentage (%)
Pantoprazole	Clobazam	4	21.05%
Phenytoin	Atorvastatin	4	21.05%
Pantoprazole	Phenytoin	3	15.78%
Carbamazepine	amlodipine	3	15.78%
Phenytoin	Clonazepam	1	5.26%
Phenytoin	Carbamazepine	1	5.26%
Atorvastatin	Metronidazole	1	5.26%
Nimodipine	Phenytoin	1	5.26%
Valproic acid	Aspirin	1	5.26%
Total		19	100%

Table 6: Medication adherence level.

Medication Adherence Level (scale) MMAS-8 Scale	Number of patients (N)	Percentage (%)
High adherence (0)	12	20.00%
Medium adherence (1-2)	9	15.00%
Low adherence (3-8)	39	65.00%
Total	60	100%

Out of 60 patients, 50 were treated with Levetiracetam as the first line of treatment. Out of which 92% had received dosage via IV route and 8% had received an oral dosage.

Mostly 2nd generation antiepileptic drugs were prescribed in 51% of the cases. 1st generation Antiepileptic drugs were prescribed in 37% of the cases and 3rd Generation Antiepileptic drugs were prescribed in 12% of the cases.

Out of 60 cases, the drugs for Antiepileptic drugs were used as monotherapy in 26 (43%) of the cases and polytherapy in 34(57%) of the cases. Out of the 34 cases in which polytherapy was prescribed. 2 Antiepileptic drugs were used in 44% of the case, 3 Antiepileptic drugs in 38% of the cases, and 4 Antiepileptic drugs in 18% of the cases.

Out of 60 patients, Antiepileptic drugs drug interaction was seen in 19 cases around 32% of the cases. Antiepileptic drugs drug interaction was severe in 53% of the cases, Moderate interaction in 16% of the cases, and Mild interaction in 32% of the cases.

Out of 19 drug interaction causes of Adverse Drug Reactions, Pharmacokinetics drug interaction was most commonly seen in 12(63%) of the cases and Pharmacodynamic drug interactions in 5(26%) of the cases and both in 2(22%) of the cases.

Out of 19 cases with drug interactions, Clobazam and Pantoprazole, Phenytoin, and Atorvastatin drug interactions were seen in 4 Cases each. Pantoprazole and Phenytoin, Carbamazepine and amlodipine drug interactions was seen in 3 Cases each. Phenytoin and Clonazepam, Phenytoin and Carbamazepine, Atorvastatin and Metronidazole, Nimodipine and Phenytoin, Valproic acid and Aspirin drug interactions were seen in a single Case each.

Out of 15 cases where Phenytoin was prescribed, It was having the most drug interactions almost in 9 cases.

The patient's responses were evaluated using 8 items Morisky Medication Adherence Scale (MMAS-8) and we found out that 65% of the patients had low adherence levels for medications and 15% had medium adherence and only 20% of the cases had high adherence of medications.

DISCUSSION

Epilepsy is a prevalent chronic neurological illness that necessitates long-term management and places a significant financial strain on the health-care system. Drug prescription patterns are frequently improper, and registering these trends is critical in an effort to improve prescribing standards. Furthermore, even if the quality of life is regarded to be less adversely damaged in those with adequate seizure control, an adult or midlife chronic epileptic illness may result in unemployment, reduced marriage rates, social isolation, and a sense of stigma.[11] While there is no cure for the disease, there are several ways for patients to control or manage their symptoms in order to enhance their quality of life, especially if the disease is detected and treated early.[12]

Several antiepileptic medications are now available, which have substantially improved seizure treatment in epileptic patients. More inventive research is needed, however, to confirm the apparent increase in tolerability afforded by many new Antiepileptic drugs. Epidemiological data analysis may be used to demonstrate which Antiepileptic drugs are more commonly administered and which are least frequently prescribed. Antiepileptic drugs that have recently entered the market and are unfamiliar to patients, as well as older drugs that have been replaced by more effective and acceptable Antiepileptic drugs, are the least used.[13]

The best strategy to treat epilepsy is to first get a diagnosis and then start therapy after that. The goal of therapy should be to use the best appropriate Antiepileptic drugs to control seizures while avoiding major adverse effects. We identified a high incidence of prescribing newer antiepileptics, sufficient use of required drugs, and few prescriptions for generic medications in this study.[14]

For the majority of epileptic patients, Antiepileptic drug medication is the basis of treatment. The main objective is to entirely prevent seizures while causing no adverse side effects, preferably with a single drug and an easy-to-follow dose plan. Patients should be well educated about the therapy plan because the response to any antiepileptic medication is unpredictable. Monotherapy is given to the vast majority of individuals with generalized seizures. The occurrence of this adverse event was decreased when compared to add-on therapy. The risks of long-term treatment with add-on therapy are increased. However, the length of treatment in monotherapy is brief, with fewer side effects. For the vast majority of cases, monotherapy treatment resulted in remission. The greatest potential outcome was achieved thanks to the patient's, physician's, and pharmacist's collaboration.

The use of two or more Antiepileptic drugs to treat epileptic patients has an extensive history However, due to fewer side effects, greater compliance, lesser teratogenicity, and cheaper cost, monotherapy has emerged as the final treatment option for both newly diagnosed and long-term patients during the last decade. Reducing Antiepileptic drugs from polytherapy to monotherapy often lessens the side effects and may enhance seizure control. For the majority of epileptic patients, Antiepileptic drug monotherapy remains the best option.

Out of 15 cases where Phenytoin was prescribed, it was having the most drug interactions almost in 9(60%) cases. A study by Magar *et al*. had similar results.[15] The most common drug with a potential causality assessment to an adverse drug response was phenytoin, which was also the sole medication with a likely causality evaluation.

The patient's responses were evaluated using 8 items Morisky Medication Adherence Scale (MMAS-8) and we found out that 65% of the patients had low adherence level for medications and 15% had medium adherence and only 20% of the cases had high adherence of medications. While Waleed *et al*. had 36% of the patients with high adherences, 49% had medium adherence and 15% had low adherence.[16]

Because of forgetfulness, non-availability, expense, exhaustion, and being away from home, compliance to Antiepileptic drugs was relatively low a high level of knowledge; thus, there is a need for increased adherence to counselling in clinics and health educational interventions to improve adherence in our rural communities where the disease cannot be managed. There is a need for more study on the relationship between clinical results and other non-drug self-management (traditional) strategies.

Intervention

Drug-related issues might be both hypothetical and realistic. Potential drug-related issues are those that will arise in the near future, whereas genuine drug-related issues have already happened. All pharmaceutical interactions were considered a possibility in our study. Actual drug-related concerns included ADR and a poor level of adherence. All of these problems were brought to the attention of the relevant physician. These were all accepted. We discussed their illness and medications with all patients who had low to moderate adherence.

Limitations

- Our research has limitations. Since its a retrospective cross-sectional study, data collection is limited.
- Because the study is based solely on single hospital records of patients, the sample size is limited, and the percentages may not be accurate approximations of the examined factors.
- Nonetheless, the study provides some insights on the most frequent kinds of epilepsy, demographic factors, and patterns of Antiepileptic drugs prescriptions among epilepsy patients in Hyderabad.

CONCLUSION

Despite the administration of an appropriate Antiepileptic drug, patients saw an increase in seizure frequency as well as the development of side effects. This problem may have been averted if a proper dose was used and polytherapy was avoided whenever possible. Given that more than half of the drugs were newer, the increased availability of newer pharmaceuticals in hospital formularies will surely lessen the financial burden of epilepsy treatment. Traditional drugs have a greater average cost than modern Antiepileptic drugs.

These data might be used by doctors and healthcare workers to make clinical decisions on how to best manage patients taking antiepileptic medicines. By using monotherapy and avoiding polytherapy if possible, side effects are reduced.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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