A Study on Trends in Prescribing Pattern of Anti-Epileptic Drugs in Teritiary Care Teaching Hospital

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ABSTRACT

Many new antiepileptic drugs (AEDs) have become available in recent years. Investigations of prescription patterns and exposure of AEDs to different patient groups are important regarding drug safety aspects. The aim of this study was to investigate the use of AEDs in epilepsy, with focus on exposure of AEDs, gender and age differences and changes in prescription patterns over time.The data was collected from 150 patients retrospectively regarding patient IDs, number of prescriptions, date of prescriptions, type of prescription, reimbursement code, age groups and gender and medication history, medical history, and demographic details of the patients was collected as for protocol. The demographic details of our study population, males 79 (52.6%) are more prone to epilepsy than the females 71 (46.3%). Generalized –tonic-clonic seizure type is the most common type of epilepsy which contribute (49.3%), and for this type of epilepsy sodium valproate was most commonly prescribed (14.6%), followed by simple partial seizure 24 (16%) and carbamazepine (13.3%) was the first line drug prescribed for simple partial seizures and complex partial seizures although phenytoin was used sporadically. Prescription patterns were consistent with current evidence about the spectrum of efficacy of individual AEDs in different epilepsy syndromes. The high prevalence of polytherapy, including combinations of three or more AEDs, is a cause for concern.

Key words: Anti epileptic drugs, Prescription, Carbamazepine, Generalized –tonic-clonic and Simple partial seizures seizure.

1. INTRODUCTION

Epilepsy (from the Ancient Greek ἐπιληψία (epilēpsía) — "to seize") is a common chronic neurological disorder characterized by recurrent unprovoked seizures. Epilepsy is the most common serious neurological disorder worldwide, affecting 50 million people [1]. Antiepileptic drugs (AEDs) consist of a variety of chemical substances, and new AEDs have been marketed during the last 20 years. There is still a lack of documentation of safety aspects regarding many of these drugs, as the use in special patient populations like children, women of childbearing age, and elderly. AEDs are drugs with considerable inter individual variability and are susceptible to cause adverse effects and drug interactions. AEDs are also extensively used in psychiatric disorders, neuropathic pain and migraine [2].

Changes in prescription patterns, exposure of specific drugs to certain patient groups, combination of drugs, generic substitution, potential for drug abuse and the use of AEDs in other disorders than epilepsy are examples of issues that may be investigated in detail using this methodology. In recent years several studies assessing the use of drugs in various populations have been published, using similar methodology restricted to subpopulations or geographical areas [3]. The purpose of the present study was to investigate the use of AEDs in patients with epilepsy in detail in the whole population, with focus on exposure of AEDs, gender and age differences and changes in prescription patterns over time, based upon data available from the prescriptions and patient information [4].

Purpose of the study is to investigate the use of antiepileptic drugs in epilepsy, Changes in prescription patterns, exposure of specific drugs to certain patient groups, combination of drugs, generic substitution, and potential for drug abuse and quantify the use of antiepileptic drugs (AEDs) in epilepsy and other disorders to be investigated in a tertiary care hospital [5].

2. METHODOLOGY

2.1. Study Material and Analyses

The study material consisted of data collection form approved by ethical committee of the institution including the following variables:

gender, patient demographic details, comarbidities, disease conditions, and details of medication, route of administration and other details of the patients, patient ID-number, and prescription description.

2.1.1. Inclusion Criteria

The study population was limited to those who were continuously eligible for the out patients and inpatients during the entire study period. Patients were identified through pharmacy drug prescriptions and the identification was for all inpatients and out patients. By hospital policy all drugs are prescribed for a maximum period of 3 months consequently, all patients presented atleast twice during the study period.

➢ Including all age group,

➢ Patient prescribed with anti epileptics and newer antiepileptic drugs.

➢ Patient diagnosed epilepsy & with other co morbidity.

➢ Patient receiving combinations of other drugs with any antiepileptic drugs.

➢ Poly therapy and monotherapy of antiepileptic treatment. Exclusion Criteria: Patient diagnosed and receiving treatment other than epilepsy.

2.2. Study Design

Prospective observational study .This study was conducted at tertiary care hospital at Erode,Tamilanadu.

2.3. Data Collection

The data was collected regarding number of patient IDs, number of prescriptions, date of prescriptions, type of prescription, reimbursement code, age groups and gender. And the demographic information like habitat, dietary intake and other parameters were collected from the patient by explaining the study protocol. The simple questions asked during the time of the data collection by participating in the ward rounds.

The data collection steps include.

➢ Preparation of the protocol of the study

➢ Preparation of simple questionary

➢ Compilation of the entire data

➢ Interpretation of the data

3. RESULTS AND DISCUSSION

Epilepsy is a common chronic neurological disorder that requires long-term management and imposes a large burden on the health-care system.[5] Drug therapy is the most commonly used method of any disease treatment

in general practice. However, the patterns of drug prescription are often inappropriate and the need for registration of these patterns is essential in an effort to improve prescribing standards [6].

Table-1: Demographic details of the patients

Demographic details of the patient	No. of the patients (150)	Percentage
Sex		
Males	79	52.6
Females	71	47.3
Age		
Paediatrics	08	10
Adults	95	60.
Geriatrics	47	30
Mariel status		
Single	23	15.3
Married	120	80
Divorced	7	4.6
Occupational status	25	16.6
Employed	34	22.6
Un employed	31	20.6
House hold	47	31.3
Farmers	12	8
Student	01	0.6
Others		

The demographic details of our study population, males 79 (52.6%) are more prone to epilepsy than the females 71 (46.3%). Epilepsy is more in the case of married persons than un married ones and unemployed labour were more prone to epilepsy than the employers (Table-1).In age wise distribution of epileptic patients 30-40yrs patient are prone to epilepsy and then followed by 40-50yrs and overall middle age people are more suffered with epilepsy compared to 60-80yrs (Table-2).

Table-2: Age wise distribution of the study population

Age	No. Of patients	Percentage
0-10	13	8.6
10-20	24	16
20-30	22	14.6
30-40	36	24
40-50	32	21.3
50-60	12	8
60-70	07	4
70-80	04	2.6

In area wise distribution of the Patients in semirural 70 (46.3%) and urban population 50 (33.3%) are more compared than rural population 30(20%) (Table-3). Generalized –tonic-clonic seizure type is the most common type of epilepsy which contribute (49.3%), and for this type of epilepsy sodium valproate was most commonly prescribed (14.6%), followed by simple partial seizure 24 (16%) and carbamazepine (13.3%) was the first line drug prescribed for simple partial seizures and complex partial seizures although phenytoin was used sporadically. The others includes complex seizure 13 (8.6%), Generalized-tonic seizure 12 (8%), myoclonic seizure 9 (6%) and Secondary generalized seizures 6(4%), followed by Absence seizure, Atonic seizures (Table-4), for these seizures commonly prescribing drug is sodium valproate.

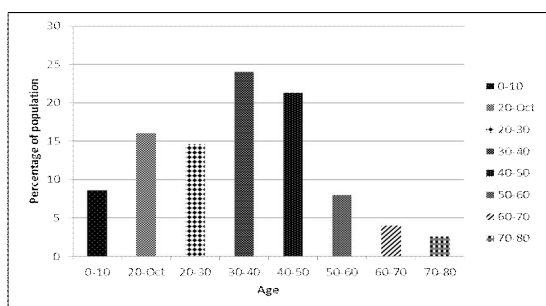Fig-2: Age wise distribution of the study population
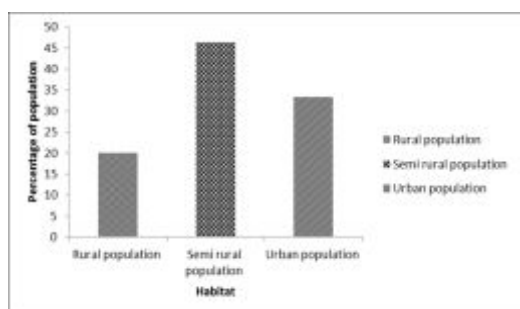

Fig -3: Area wise distribution of patients

Table- 3: Area wise Distribution of epileptic patients

Habitat	No. Of patients (150)	Percentage
Rural population	30	20
Semi rural population	70	46.3
Urban population	50	33.3

Table -4: Classification of epileptic seizures

Classification of seizures No. Of patients(150)	No of patients	Percentage
Generalized-tonic-clonicseizure	74	49.3
Generalized-tonic seizure	12	8
Generalized-clonic seizure	4	2.6
Absence seizure	6	4
Myoclonic seizure	9	6
Atonic seizures	2	1.3
Simple partial seizures	24	16
Complex seizures	13	8.6
Secondary generalized seizures	6	4

Cryptogenic epilepsy 111 (74%) was the most common cause of epileptic seizures, followed by idiopathic, 12 (8%) trauma/head injury 5 (3.3%), infection 5 (3.3%) and systemic disease 5 (3.3%), metabolic disorder 6 (4%) and toxic accounted for 6 (4%) of all causes (Table-5). Monotherapy 82 (54.6%) was commonly used for the treatment of epilepsy sodium valproate (14.65) and phenytoin (30%) are commonly prescribed monotherapy, followed by other drugs like in dual therapy 47 (31.3%) topiramate with carbamazepine or phenytoin, and three anti epileptic drug combinations 14 (9.3%) are phenytoin with sodium valproate and etosuximide.Four drug combinations 7 (4.6%); phenytoin, carbamazepine, sodium valproate, lamotrigine, were prescribed (Table-6).
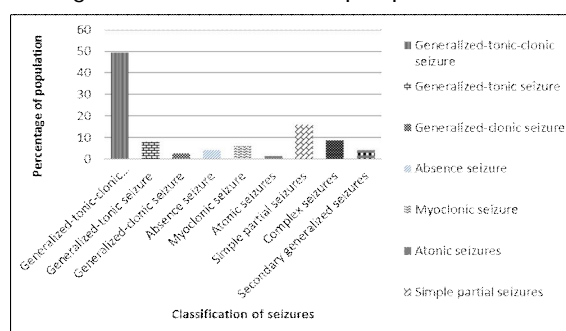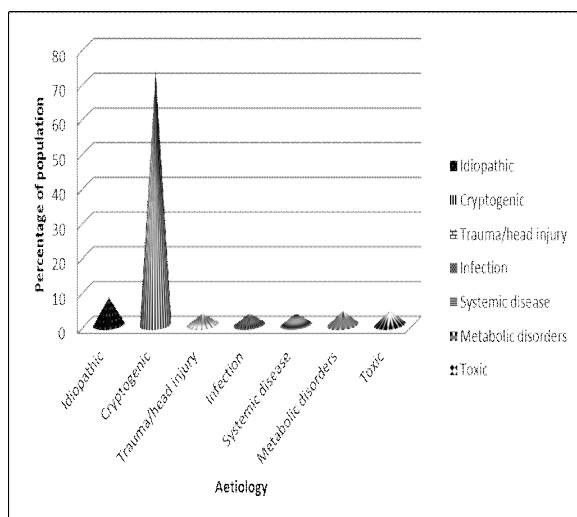
Fig -4: Classification of epileptic seizures

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Table -5: The etiology wise distribution of epileptic seizures

Aetiology	No. Of patients (150)	Percentage
Idiopathic	12	8
Cryptogenic	111	74
Trauma/head injury	5	3.3
Infection	5	3.3
Systemic disease	5	3.3
Metabolic disorders	6	4
Toxic	6	4

Fig -5: Etiology wise distribution of study population

Unlike the subjects included in other pharmacoepidemiological studies, our study population was characterized by its middle age. Almost 48% of the patients were between 31and 60 [7]. In our study, the lack of a peak in the elderly was probably because of the relative young and middle age of our study population. Generalized tonic clonic seizures followed by simple partial seizures were the most common type of epileptic seizures encountered in our study. The key to treating epilepsy is correct diagnosis of the seizure type. Most patients with epilepsy respond to one of the first-line antiepileptic drugs; second line agents may be useful in patients who do not respond to one or a combination of the first-line agents [8]. The selection of antiepileptic drugs (AEDs) is increasingly more complex as new agents become available. The best antiepileptic therapy is dependent on optimal seizure control and absence of unacceptable side effects.

Table- 6: Utilization of anti epileptic drugs

Antiepileptic drug therapy	No. Of patients (150)	Percentage
Monotherapy	82	54.6
Dual therapy	47	31.3
Three drug therapy	14	9.3
Four drug therapy	07	4.6

Fig - 6: Utilization of antiepileptic drugs
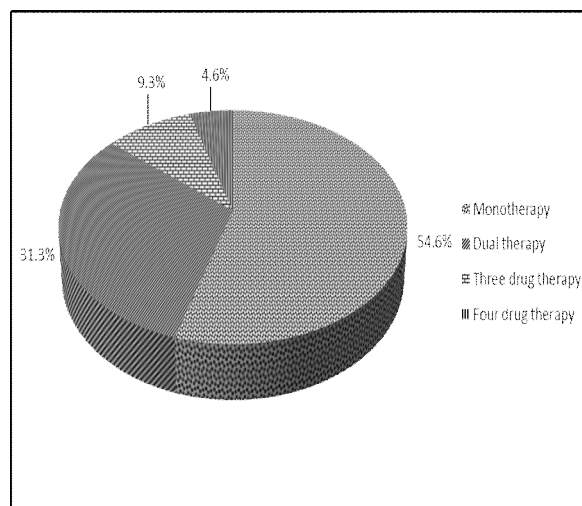
Phenytoin is the most commonly used drug for the treatment of epilepsy in our study 45 (30%), followed by sodium valproate 22 (14.6%) and carbamazepine 20 (13.3%) and other drugs also used as some times monotherapy, or in combinations with other drugs like Topiramate 10 (6.6%), phenobarbitone 8 (5.3%), clonazepam 7 (4.6%) and lamotrigine 6 (4%), Oxcarbazepine, clobazam, and Gabapentene (Table-7). Hematological disturbances 26 (17.3%) are most common side effects of anti epileptic drugs of our study, followed by electrolyte disturbances 21 (14%) and dermatological disturbances 21 (14%) and others like shortness of breath, hepatic disturbances (Table-8).

Table -7: Classification of anti-epileptic drugs prescribed among study population

Antiepileptic drug therapy	No. Of patients (150)	Percentage
Sodium valproate	22	14.6
Carbamazepine	20	13.3
Phenytoin	45	30
Lamotrigine	6	4
Clonazepalm	7	4.6
Phenobarbitone	8	5.3
Topiramate	10	6.6
Oxcarbazepine	5	3.3
Clobazam	4	2.6
Gabapentene	5	3.3
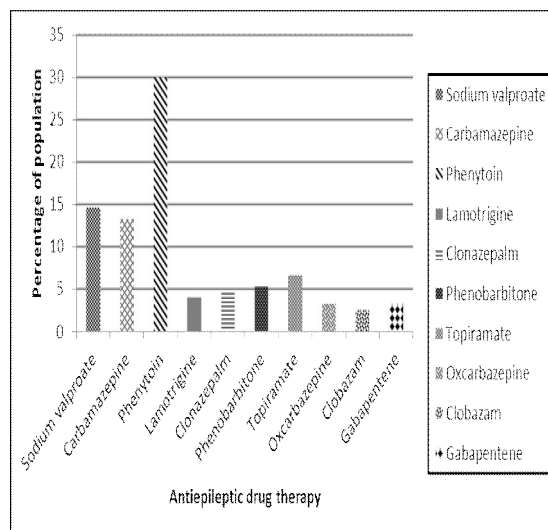
Table -8: Classification of side effects among study population

Side effects	No. of patients (150)	Percentage
Hematological disturbances	26	17.3
Electrolyte disturbances	21	14
Hepatic disturbances	18	12
Weight loss	13	8.6
Shortness of breath	19	12.6
Gastric disturbances	4	2.6
Dermatological disturbances	21	14
Hair changes	5	3.3
Cognitive disturbances	11	7.3
Sedation	12	8

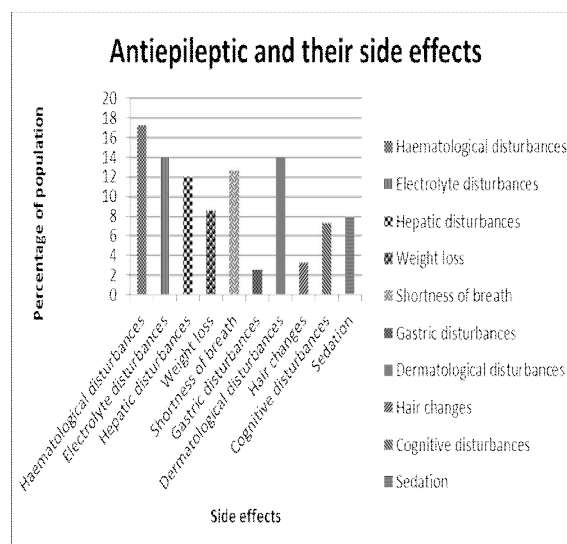Fig -7: Classification of anti-epileptic drugs prescribed among study population

Fig – 8: Classification of side effects among study population

Psychometric tests were developed, with good control of conditions, and hence were useful for comparisons. However, the natural course of the seizure disorder is unpredictable, so severity, seizure control, and prognosis cannot easily be overviewed at the time of diagnosis. Previous studies demonstrated that people with epilepsy may be prone to lower self-esteem and a higher incidence of anxiety and depression, compared with subjects without seizures [9-10].

Moreover, unemployment, lower marriage rates, social isolation, and the feeling of stigmatization may follow an adult or midlife chronic epileptic condition, even if the quality of life is thought to be less severely affected in people with good seizure control [11]. The wide use of newer AEDs in indications other than epilepsy

is in line with other studies that documented an increased use of newer AEDs in the last few years for the treatment of neuropathic pain [12-13]. However, users of older AEDs were significantly more affected by epilepsy compared with newer AED users.

The finding that there was higher number of prescriptions with AEDs for male patients compared to female patients is in parallel with previous reports. This differential gender distribution may be attributed to an increased incidence of head trauma in males responsible for post traumatic epilepsy [14]. It is well established that lesser number of drugs per prescription minimizes risk of adverse drug reactions, drug interactions and the treatment costs. In the present study, polypharmacy data revealed acceptable findings. There were the highest number of prescriptions with one drug, fewer numbers with more than five drugs, indicating the recommended limits of polypharmacy and thus rationality in therapeutic practices [15].

A majority of the prescriptions (54.6%) had a single AED (monotherapy) prescribed, which is in line with rational therapeutics particularly considering the cost of therapy for developing country like ours. This is because sometimes even the low cost of phenytoin and Phenobarbitone is not affordable by many. A small proportion (4.6%) of prescriptions had combination of AEDs (polytherapy) which may be related to their use in refractory seizures. The use of two drug combinations with different mechanisms of action complementary to one another has, however, been reported to be beneficial to patients [16]. The most commonly prescribed combination in the Present study was phenytoin with Phenobarbitone, which is widely accepted.

In our study, sodium valproate was the first-line drug prescribed in generalized seizures, followed by carbamazepine and phenytoin. Carbamazepine and sodium valproate were the AEDs of choice for the treatment of partial seizures [17]. In this study group, sodium valproate was most commonly prescribed for the treatment of generalized tonic-clonic seizure, generalized tonic seizure, generalized clonic seizure, absence, atonic and myoclonic seizures [18]. In our study carbamazepine was the first line drug prescribed in simple partial seizures and complex partial seizures, although phenytoin was used sporadically. Increasing evidence suggests that valproic acid is a good alternative when carbamazepine and phenytoin fail [19].

Monotherapy was the therapy of choice in the majority of patients with partial or generalized seizures. Polytherapy offers no advantage over monotherapy. It increases the potential for drug-drug interactions [20], results in failure to evaluate the individual drugs, can increase the risk of chronic toxicity (including neurocognitive problems, may affect compliance and is associated with a higher cost of medication and the necessity for therapeutic drug monitoring (TDM)). Despite this, polytherapy may be the only way of achieving improved seizure control in only 10% of patients with epilepsy [21].

Considering all types of generalized seizures phenytoin was the most frequently prescribed AED, followed by sodium valproate. In partial seizure carbamazepine followed by phenytoin were the most frequently prescribed AEDs [22]. A first line AED should be one, such as valproic acid, with a broad spectrum of activity that is easily managed by clinicians who may not have special expertise in the recognition of differing seizure types and epileptic syndromes.

Our study shows that most epileptics can be effectively managed with the conventional AEDs. Patients in good control need not be seen more frequently than every four to six months if they had no seizures for a six- month period.23 Patients whose seizure control is fair or poor should be assessed for medication adherence and other exacerbating factors. Physicians should consider placing patients on directly observed therapy (DOT) when serum levels are low and patient experience seizures [23].

Drug-drug interactions between AEDs and other groups of drugs due to enzyme induction or enzyme inhibition have been reported, leading to toxicity or lack of response as a result of an increase or decrease in serum levels of AEDs following concomitant administration of drugs [24]. Such harmful combinations, although infrequent in the present study, require careful attention as they could be of clinical significance. However, it may be suggested that these issues be brought up in clinical meetings and during interactive sessions to improve awareness, and understand the consequences of harmful drug combinations and formulate necessary guidelines to avoid drug interactions.

As the ADR data were retrieved from patient medical records, it is very likely that ADR reporting was under estimated. Most accurate data could have been obtained by questioning the patient directly.

The standard AEDs such as carbamazepine, phenytoin and sodium valproate have been shown to have equivalent efficacy in the management of epileptic seizures [25]. A more favorable pharmacokinetic profile is observed in

the majority of the newer AEDs in contraposition to the classic agents. Good absorption linear kinetics and low drug-drug interaction potential make these drugs easier to use [26].

Newer AEDs, used as monotherapy, may be cost-effective for the treatment of patients who have experienced adverse events with older AEDs who have failed to respond to the other drugs, or where such drugs are contraindicated. In our study the limited prescribing of new generation AEDs indicated that these drugs are still relatively under used.

Oxcarbazepine was found to be the most frequently prescribed AED for non-epileptic problems, followed by gabapentin. Newer anticonvulsants such as Oxcarbazepine may offer improved tolerability and fewer drug-drug interactions compared to older drugs like carbamazepine [5].

4. CONCLUSION

The study is concluded that generalized seizures were more prominent, probably explaining the unique drug utilization profile. Monotherapy was most frequently used in all types of epileptic seizures. Particularly monotherapy was the choice in the majority of patients with partial or generalized seizures. Polytherapy offers no advantage over monotherapy. It increases the potential for drug-drug interactions; results in failure to evaluate the individual drugs. The selection of the AEDs corresponds well with the known efficacy profile for specific epileptic seizure types. The most commonly prescribed AED as sodium valproate, followed by carbamazepine, phenytoin for epilepsy. Oxcarbazepine, phenytoin was prescribed for non-epileptic problems. Most epileptics can be effectively managed with the conventional oral AEDs.

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