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Assessment of prescription pattern on anti-epileptic drugs used in epilepsy patients in a tertiary care corporate hospital

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ABSTRACT

Background & Objectives

Epilepsy is characterized as the repeated occurrence of sudden synchronous discharge of cerebral cortical neurons. Anti-epileptic drugs (AEDS) treatment is based on patient specific and seizure specific considerations. The main objectives of this study is to assess the anti-epileptic drugs use in tertiary care hospital & to classify the type, etiology of seizures, analysing the prescription pattern ,categorisation & combinations of Anti-epileptic drugs, assessing age & gender specific distribution, pharmacoeconomics in epilepsy management.

Methodology

A prospective observational study using patient medical records and the necessary data were collected by using data collection forms and results were evaluated against the criteria prepared from the standard treatment guidelines.

Results

Prescription of 200 patients were studied & analysed. The demographic data revealed that there are 81(40.5%) female patients and 119 (59.5%) male patients respectively.

Dual therapy was used in majority of patients. Conventional drugs were used in more frequency than newer drugs.

Conclusion

In conclusion, our study on the prescription pattern of AEDs shows that male gender was more prone to epilepsy. Unlike in other similar studies, dual therapy was mostly prescribed. It shows that the most common combination was LEVETIRACETAM and PHENYTOIN which shows that the combination of an older drug and newer drug would improve patient condition. The study concludes that adjuvant therapy with anti-epileptic drugs gives better results. Lack of specific guidelines for the usage of AED in India, the rationality in the prescription is poor and variable.

Keywords: Prescription pattern of AEDS, Dual therapy, Adjuvant therapy

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INTRODUCTION

Objectives of the study

Primary objective

To assess the prescription pattern of antiepileptic drugs in epilepsy patients in a tertiary care corporate hospital.

Secondary objectives

- To evaluate information regarding type, risk factors of different forms of seizures.
- To describe important characteristics of different anti-epileptic drugs.
- To discuss regarding more frequent combinations of anti epileptic drugs.
- To assess prescription pattern.
- To assess age specific and gender specific distribution of anti-epileptic drugs.

METHODOLOGY

This is a prospective and observational study. A protocol was prepared and submitted, which was approved by Institutional Ethics Committee of Sunshine hospitals, Secunderabad, which is a Multi-super specialty tertiary care hospital. In this study 200 patients were enrolled after obtaining the consent. The data collection form was prepared and used. This form mainly contains the demographic details of the patient, medication history, diagnosis and treatment of the patient.

This study was carried out in In-patient department (IPD) of Sunshine hospitals, Secunderabad, which is a 500+ bedded Multi-super specialty tertiary care hospital. Patients from pregnant and lactating women, and pediatrics were excluded from our study. Randomly 200 patients were enrolled in to the study based on study criteria. A self-designed patient data collection form was developed and used for this study. Patient records from the inpatient ward were obtained. A total of 200 prescriptions prescribed with anti-epileptics written by qualified medical doctors were collected from wards and analysed. Latest edition of DRUG TODAY manual was used to decode brand name of drugs to generic names for the purpose of analysis. Data was analyzed using descriptive statistics namely total numbers, percentage, mean and chi-square test wherever applicable. Microsoft word and Excel have been used to generate graphs, tables etc. After data collection it was analysed for statistical significance.

RESULTS

Table 1: Gender wise distribution

GENDER	NO. OF PATIENTS	PERCENTAGE
MALE	119	59.5
FEMALE	81	40.9

Table 2: Age wise distribution

AGE	19-20	21-30	31-40	41-50	51-60	61-70	71-80	81-80	TOTAL
N	08	**54**	23	23	31	35	23	**03**	200
n	04	**27**	11.5	11.5	15.5	17.5	11.5	**1.5**	100

N=Number of patients, n=Percentage of number of patients.

Table 3: Age-gender correaltion:

AGE	MALE (N)	n%	FEMALE (N)	n%
19-20	03	02.52	05	06.17
21-30	**26**	**21.8**	**28**	**34.56**
31-40	11	09.24	12	14.81
41-50	16	13.44	07	08.64
51-60	24	20.16	07	08.64

61-70	24	20.16	11	13.58
71-80	14	11.76	09	11.11
81-90	**01**	**0.84**	**02**	**02.46**

N=Number of patients, n= Percentage of number of patients.

Table 4

GENDER	MEAN AGE	MINIMUM AGE	MAXIMUM AGE
MALE	50	19	85
FEMALE	43	19	85

Table 5: risk factors of seizures

SL.NO	RISK FACTORS	N	n
1	CRYPTOGENIC	**76**	**38**
2	IDIOPATHIC	48	24
3	SYSTEMIC DISEASES	32	16
4	METABOLIC DISORDERS	19	9.5
5	INFECTIONS	15	7.5
6	HEAD INJURY	07	3.5
7	TOXICITY	**03**	**1.5**

N=Number of patients, n= Percentage of number of patients

Table 6: classification of epileptic seizures

SL.NO	TYPE OF SEIZURE	N	n
1	GENERALIZED TONIC CLONIC SEIZURES	**78**	**39**
2	GENERALIZED TONIC SEIZURES	10	05
3	ABSENCE SEIZURES	20	10
4	MYOCLONIC SEIZURES	13	6.5
5	ATONIC SEIZURES	08	04
6	SIMPLE PARTIAL SEIZURES	18	09
7	COMPLEX PARTIAL SEIZURES	22	11
8	SECONDARY GENERALIZED SEIZURES	**07**	**3.5**
9	SIMPLE FEBRILE SEIZURES	14	07
10	COMPLEX FEBRILE SEIZURES	10	05

N=Number of patients, n=Percentage of number of patients.

In the present study, a total of 352 anti epileptic drugs (AEDS) were prescribed to 200 patients. Average number of AEDS per patient = Total number of AEDS / Total number of patients= 1.76. The most commonly prescribed AED in our study was levetiracetam and least the prescribed was phenobarbitone. To study the utilization pattern of AEDS, the drugs were prescribed as mono therapy, dual therapy, triple therapy and poly therapy.

Table 7: Pharmaco-epidemiologic data

TYPE OF THERAPY	N	FREQUENCY
MONO THERAPY	83	41.5
DUAL THERAPY	**86**	**43**
TRIPLE THERAPY	24	12
POLY THERAPY	**07**	**3.5**

Table 8: Mono therapy prescription pattern

DRUG	N	N
LEVETIRACETAM	**52**	**62.65**
PHENYTOIN	18	21.6
LAMOTRIGINE	**01**	**01.2**
SODIUM VALPROATE	05	06.02
CLOBAZAM	06	07.22
CARBAMAZEPINE	**01**	**01.2**

N=Number of patients, n= Percentage of number of patients.

Table 9: Dual drug therapy distribution

DRUG COMBINATION	N	n
LEVETIRACETAM +PHENYTOIN	**36**	**41.8**
LEVETIRACETAM +SODIUM VALPROATE	09	10.4
LEVETIRACETAM + CLOBAZAM	15	17.4
LEVETIRACETAM +CARBAMAZEPINE	03	03.4
LEVETIRACETAM + GABAPENTIN	02	02.32
LAMOTRIGINE + PHENYTOIN	03	03.4
LAMOTRIGINE + SODIUM VALPROATE	03	03.4
LAMOTRIGINE + CARBAMAZEPINE	05	05.81
PHENYTOIN + CLOBAZAM	07	08.13
PHENYTOIN + CARBAMAZEPINE	02	02.32
PHENYTOIN + TOPIRAMATE	**01**	**01.16**

N = Number of patients, n = Percentage of number of patients.

Table 10: Triple therapy drug distribution

DRUG COMBINATION	N	n
LEVETIRACETAM + PHENYTOIN+CLOBAZAM	**11**	**45.8**
LEVETIRACETAM + PHENYTOIN + CARBAMAZEPINE	03	12.5
LEVETIRACETAM + SODIUM VALPROATE + CARBAMAZEPINE	03	12.5
LEVETIRACETAM + CLOBAZAM + CARBAMAZEPINE	02	08.3
LAMOTRIGINE + PHENYTOIN + CLOBAZAM	02	08.3
LAMOTRIGINE + SODIUM VALPROATE + CLOBAZAM	02	08.3

PHENYTOIN + PHENO BARBITONE + CARBAMAZEPINE	**01**	**04.16**

N = Number of patients, n = Percentage of number of patients

Table 11: Poly therapy drug distribution

DRUG COMBINATION	N	n
LEVETIRACETAM + PHENYTOIN+CLOBAZAM+CARBAMAZEPINE	**04**	**57.14**
LEVETIRACETAM +SODIUM VALPROATE+CLOBAZAM+TOPIRAMATE	02	28.57
LEVETIRACETAM+SODIUMVALPROATE+CLOBAZAM+CARBAMAZEPINE	**01**	**14.28**

N = Number of patients, n = Percentage of number of patients.

Table 12 : Comparison of mono therapy, Dual Therapy, Triple therapy and poly therapy with age

TYPE OF THERAPY	19-20	21-30	31-40	41-50	51-60	61-70	71-80	81-90
MONO THERAPY	**03**	**20**	08	10	08	17	14	**03**
DUAL THERAPY	03	**24**	14	08	18	14	05	**00**
TRIPLE THERAPY	01	**09**	01	03	04	02	04	**00**
POLY THERAPY	01	01	**00**	**02**	01	**02**	**00**	**00**

Table 13: Route of anti epileptic drugs administration

ROUTE	NUMBER OF PATIENTS	PERCENTAGE
ORAL	268	75.9
INTRA VENOUS	84	24.07

Anti epileptic drugs can be categorized into two groups:

1. Old Anti epileptic drugs: These includes phenytoin, clonazepam, sodium valproate, carbamazepine, phenobarbitone etc.
2. New Anti epileptic drugs: These include gabapentin, topiramate, lamotrigine. levetiracetam, oxcarbamazepine etc .

Table 14: Prescription pattern

OLDER DRUGS	N	NEWER DRUGS	N
PHENYTOIN	85	LEVETIRACETAM	136
SODIUM VALPROATE	26	LAMOTRIGINE	15
CARBAMAZEPINE	17	GABAPENTIN	04
PHENO BARBITONE	01	OXCARBAMAZEPINE	08
CLONAZEPAM	57	TOPIRAMATE	03

N= Number of patients.

Table 15: Utilization pattern of older aeds, newer aeds and the combination of older and newer aeds according to age

AGE	OLDER AEDs	NEWER AEDs	OLDER+NEWER AEDs
19-30	**11**	13	38
31-50	09	**10**	27

51-70	08	**19**	**39**
71-90	**06**	11	**09**

Table 16: Adjuvant therapy

Benzodiazepines were used as adjuvant therapy to treat epilepsy. In our study clobazam**,** clonazepam, lorazepam were commonly prescribed as an adjuvant therapy.

DRUG COMBINATION	N	N
BENZODIAZEPINES ONLY	**06**	**10.5**
BENZODIAZEPINES + 1 ANTI EPILEPTIC DRUG	**26**	**45.6**
BENZODIAZEPINES + 2 ANTI EPILEPTIC DRUGS	19	33.3
BENZODIAZEPINES + 3 ANTI EPILEPTIC DRUGS	07	12.2

N = Number of patients, n = Percentage of number of patients

DISCUSSION

A total of 200 prescriptions of epileptic patients with anti-epileptic drugs have been analyzed for the study. The study describes the utilization pattern of different AEDs with demographic characteristics and pharmaco-epidemic data of epileptic patients. It was completely a prospective observational study, conducted in a tertiary care hospital for the duration of six months. The aim of AED therapy is to stop the occurrence, reduce the frequency of epileptic seizures with minimal adverse effects and to improve the quality of life of the patient. The selection of specific anti epileptic drug / drugs is primarily dictated by efficacy in attaining full control of seizures. By gender wise distribution, it was revealed that male predominance over female patients. Out of 200 patients, number of male patients were 119 (59.5 %) and female patients were 81 (40.9%).Several other similar literatures also states that number of male patients were more than female patients. The reason behind the gender difference was not clear. But, it supposes that estrogen has a seizure activating effect whereas progesterone shows seizure protective effect.

Age distribution of the study population revealed that maximum number of patients were between 21-30(27%), followed by 61-70(17.5%), 51-60(15.5%), 31-40(11.5%), 41-50(11.5%), 71-80(11.5%), 19-20(4%) and the least number of patients were in the age group of 81-90(1.5%). In our study, the minimum age of patient suffering with epilepsy was 19 and maximum age of patient was 85. On correlating age and gender distribution in the study, it was concluded that maximum incidence of epilepsy in male patients was between the age group 21-30 years, followed by 51-60 years,61-70 years,41-50 years,71-80 years,19-20 years and minimum incidence was between the age group of 81-90 years.

Among the female patients, the maximum incidence of epilepsy was between the age group 21-30 years, followed by 31-40 years,61-70 years,71-80 years,41-50 years,51-60 years,19-20 years and the minimum incidence was between the age group 81-90 years. It was found that there was significant difference between age and gender in terms of incidence of seizures which shows p value 0.029208 with level of significance 0.005 and chi-square value 9.0062. The average (mean) age of onset of epilepsy in male patients was 50 years whereas in female patients, it was found to be 43 years. The minimum age of onset of epileptic seizures in our study in both genders was 19 years and maximum age of onset was 85 years. By assessing risk factors, it was revealed that cryptogenic epilepsy was most common risk factor of epileptic seizures (38%),followed by idiopathic (24%),systemic diseases (16%),metabolic disorders (9.5%),infections (7.5%) ,head injury (3.5 %) and toxicity of 1.5% .

The maximum number of patients were diagnosed with GTCS (39%) , followed by complex partial seizures (11%), absence seizures (10%),simple partial seizures (9%),simple febrile seizures (7%), myoclonic seizures (6.5%),complex febrile seizures (5%),generalized tonic seizures (5%), atonic seizures (4%) and the minimum number of patients were diagnosed with secondary generalized seizures (3.5%). Our studies were similar to the reports from most of the Asian countries, where the generalized seizures ranges from 50-60% and partial seizures of about 31-50%.It was difficult to compare the results of these studies due to lack of imaging and EEG

studies which led to predominance of generalization in most of the studies. In this study, the average number of antiepileptic drugs prescribed per patient were 1.76. None of the anti-epileptic drugs were prescribed in generics, despite the fact was that generics are comparatively less expensive and helps in reducing health care costs.

Dual therapy was most commonly prescribed type of therapy, followed by mono therapy, triple therapy and poly therapy. Among the mono therapy, levetiracetam was most frequently prescribed of about 62.6%, followed by phenytoin (21.6%) ,clobazam (7.22%),sodium valproate (6.02%),lamotrigine and carbamazepine was least prescribed as monotherapy of about 1.2%. Among the dual therapy , the most commonly prescribed combination was levetiracetam and phenytoin (41.8%),followed by levetiracetam and clobazam (18%),levetiracetam and sodium valproate (11%),phenytoin and clobazam (8%),lamotrigine and carbamazepine (6%),levetiracetam and carbamazepine (4%),lamotrigine and phenytoin (3%),lamotrigine and sodium valproate (3%) ,phenytoin and carbamazepine (2%), levetiracetam and gabapentin (2%) whereas the least commonly prescribed dual drug combination were phenytoin and topiramate (1%).

The most frequent triple therapy combination were levetiracetam with phenytoin and clobazam (46%), followed by levetiracetam with phenytoin and carbamazepine (13%), levetiracetam with sodium valproate and clobazam (13%). It was followed by levetiracetam with clobazam and carbamazepine (8%) , lamotrigine with phenytoin and clobazam (8%), lamotrigine with sodium valproate and clobazam (8 %) and the least prescribed combination were phenytoin with phenobarbitone and carbamazepine (1%).

Only 7 patients were prescribed with more than 3 drugs (polytherapy) in our study population during the period of six months. Among them, the most common poly therapy combination was levetiracetam with phenytoin, clobazam and carbamazepine of about 57 %. It was followed by levetiracetam with sodium valproate ,clobazam and topiramate(29%).The least prescribed combination of drugs in poly therapy were about 14% by levetiracetam with sodium valproate , clobazam and carbamazepine.

On comparision of mono therapy, dual therapy, triple therapy and poly therapy with age, mono therapy was most frequently prescribed in patients between the age group 21-30 years and less commonly prescribed in patients between the age group 81-90 years .Dual therapy was prescribed maximum in patients between the age group 21-30 years and minimum in patients with the age above 80 years.

Triple therapy was most commonly prescribed in the patients between the age group 21-30 years and less in patients above 80 years. Poly therapy was less frequently prescribed type of therapy compared with other therapies. It was highly prescribed in patients between the age groups 41-50 years and 61-70 years. Poly therapy was less frequently prescribed in patients between the age groups 31-40 years,61-70 years,71-80 years and in 81-90 years.

It was found that there was no significant difference between type of therapy and age of the patients as p value shows 0.7472 and chi-square value 1.2238 with 0.005 as level of significance. Oral anti-epileptic drugs were mostly prescribed than intravenous anti-epileptics. Old/ conventional anti-epileptic drugs were prescribed in higher frequency than newer drugs. It may be due to higher cost and non-availability in government supply of newer drugs. There was a significance difference between prescribing older drugs, newer drugs and combination of older and newer drugs in terms of age as p value shows 0.0042 with level of significance 0.005.

Benzodiazepines were used as adjuvant therapy to treat seizures. Clobazam and clonazepam were commonly prescribed adjuvant drugs. Benzodiazepines were more commonly given with single anti epileptic drug (45%),followed by combination with two anti epileptic drugs (33%) ,combined with three anti epileptic drugs (12%) . Only benzodiazepines were given in about 10% of the sample population.

It was found that there was a significant difference between the use of only anti-epileptic drugs and combination of benzodiazepines with anti-epileptic drugs as p value shows 0.042 which suggests that the addition of benzodiazepines to anti-epileptic therapy will improve the patient condition.

CONCLUSION

In our study on the prescription pattern of AEDs, it was found that that male gender was more prone to epilepsy. A significant relation occurs between age and gender for the incidence of epilepsy. There was large number of generalized seizures followed by partial seizures. Due to lack of proper imaging and EEG studies the predominance of generalization occurs in most of the studies. Most of the drugs were prescribed from the essential drug list or formulary and the prescription pattern was influenced by the drug availability in hospital pharmacy and the economic status of the patients. Unlike in other similar studies, dual therapy was mostly prescribed. Levetiracetam and phenytoin was the most frequent combination used to treat epileptic seizures in dual therapy which shows that the combination of an older drug and newer drug would improve patient condition.

Conventional anti-epileptic drugs were prescribed in higher frequency than newer drugs.It may be due to higher cost and non-availability in government supply of newer drugs. The study concludes that adjuvant therapy with anti-epileptic drugs gives better results. Benzodiazepines were used as adjuvant therapy to treat seizures. On the addition of Benzodiazepines to anti-epileptic therapy, the patient health condition can be improved. None of the anti-epileptic drugs were prescribed in generic name. In order to achieve rational drug use , drugs must be prescribed in generic names. Hence, it was concluded that lack of specific guidelines for the usage of AED in India, the rationality in the prescription is poor and variable.

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