Drug Utilization Evaluation of Antiepileptic Drugs in a Tertiary Care Hospital

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Abstract: _Background & Objectives: Epilepsy is characterized by repeated seizures due to disorder of the brain cells. Antiepileptic drugs (AEDs) treatment based on patient specific consideration including adverse effects. The objective of present study to evaluate antiepileptic drugs use in an outpatient epilepsy clinic in a tertiary care hospital and classify the seizure, analyse drug utilization pattern, categorization of AEDs, assessment of tolerability, drug interactions and contraindication. Materials and methods: A retrospective drug use evaluation using patient medical records and the necessary data's were collected by using data collection formats and results were evaluated against the criteria prepared from the standard treatment guidelines. Results: 114 patient's records were studied and simple partial seizures (27.2%) were found most common type of epileptic seizure. Conventional antiepileptic drugs were given for the majority patients (34.2%) and headache (19.2%) was commonest adverse effect reported. The most commonly prescribed drugs were Levetiracetam (44.7%), which was given mostly for simple partial seizure (41.1%), followed by Carbamazepine and Clobazam(26.3%)andpotential drug-drug interactions were also reported as 36.8% cases.Conclusion:This study suggests the dynamic role of a clinical pharmacist in the review of drug use in hospitals and the importance of DUE program as tool for improving clinical care rather than a budget plan._

Keywords: Epilepsy, Antiepileptic drugs, Retrospective evaluation, Drug utilization

1. Introduction

Epilepsy is a condition characterized by repeated seizures due to a disorderof braincells [1]. Polytherapy can be considered when monotherapy (with 2 or 3 agents) fails at maximal tolerated doses, and is preferred more [2]. Standard Antiepileptic drugs(AEDs) such ascarbamazepine, phenytoin and sodium valproate are commonly used for patients with newly diagnosed epilepsy. Newer AEDs such aslacosamide, lamotrigine, levitiracetam, oxcarbazepine, topiramate, zonisamide are used as add-on therapy in patients with partialonset seizures who do not respond to other AEDs. Epilepsyaffectsalmost 10 million people in India [3]. Status epilepticus is a serious and potentially life-threatening complication of epilepsy [4].It is mostly observed in children below 3years age group with a decreasing frequency in older children.The distribution of epilepsy in the population is not uniformacross age groups [5].The incidence has been estimated at between 20 and 70 cases per 100,000 persons per year, and the cumulative incidence at 2–5%. Problems in use of medicines suggest a need for DUE(Drug Utilization Evaluation) which includeshigh number of Adverse Drug Reactions (ADRs), treatment failures and excessive number of non-formulary medications, use of high-cost medicines where less expensivealternatives exist, excessive number of medicines within a therapeutic category[6].DUEis defined as an authorized, structured, ongoing review of healthcare provider prescribing, pharmacist dispensing, and patient use of medication.Toimprove the use of medicines byimproving prescribing and educational, managerial, and regulatory interventions feedback to prescribers is necessary[7].Antiepileptic drug use evaluation is a paramount importance in identifyingproblem area for intervention.

Main goal of the present study is to categorize different type of seizures, describe the drug utilization/prescription pattern of antiepileptic drugs for the treatment of various epileptic seizures with standard treatment guidelines, evaluate the tolerability of antiepileptic drugs, evaluate the extend of contraindication considered in using anti-epileptic drugs, to assess the drug-drug interaction for administered drugs and provides baseline information for responsible bodies for monitoring and regulating their drug use pattern.

2. Materials and Methods

Study site: Epilepsy clinic in the Department of Neurology, a 350 bedded tertiary care private hospital [P.V.S.Hospital(P) LTD, Calicut (Ref.No: PVS/EC/02/16-17)].

Study design: A retrospective drug use evaluation using patient medical records. The necessary data were collected from patient medical cards by using data collection form and the result was evaluated against the criteria prepared from the standard treatment guidelines.

Study period: The retrospective drug utilization evaluation study was conducted over a period of six months(December 2015- May 2016).

Study sample: 114 patients.

Study criteria: All epileptic patient medical records which fulfill study criteria in the epilepsy outpatient clinic.

Inclusion criteria: All epileptic patient cases (irrespective of age, gender and presence of concurrent diseases) treated in outpatient clinic.

Exclusion criteria: All illegible, incomplete and improperly written prescriptions as well as inpatient epileptic patients.

Data Sources: Epileptic outpatientdata's were collected from:
a) Patient data collection form
b) Patient case history and medication history documentation forms.
c) Patient prescriptions and treatment chart record files.

3. Methodology

- Datas were collected from outpatient filing area and entered into data collection form.
- Collected patient's demographic data were tabulated into sex, age, educational status, family history of epilepsy among relatives and marital status.
- Classifications of seizures were done in comparison with number of patients from the collected disease details.
- Initial onset of epilepsy attack was tabulated based on age.
- Presence of other comorbid conditions in epileptic patients was checked.
- Antiepileptic Drug Utilization was expressed as prescription pattern (mono therapy, dual therapy, triple therapy and poly therapy).
- Number of drug interactions present among the collected patient data's was checked.
- AEDs categorization into newer, conventional and conventional/newer drugs done.
- ADRs were observed in patients was recorded.
- AEDs use profile as a function of the type of epileptic seizure represented.
- Utilization of each specific AEDs in different type of seizures wastabulated.

4. Results and Discussion

Socio-demographic characteristic of patients with the antiepileptic drugs is shown in Table-1.The resultsindicated that 63(55.3%) were males and the rest were females. The dominant age group of this study was 19-65 years reported as 53 patients (46.5%) followed by 40(35.1%) from 5-18 years.This result indicates that the study population was characterized by young and middle age. These results were in accordance with a study done on drug use evaluation of antiepileptic drugs in outpatient epilepsy clinic in Ethiopia by Wakjira Rishe*et al*[8]classification of epileptic seizure is shown in Table-2 showssimple partial seizure 31(27.2%) were the most common type of epileptic seizure encountered. This result is in accordance with a study done on drug utilization evaluation of anti-epileptics in three selected multidisciplinary teaching hospitals of Pakistan by Faizan Mazhar *et al*[9].

Onset of initial epilepsy attack is shown in Table-3 shows age wise distribution of onset of initial epilepsy attack. Majority initial attack found to be in less than 5 years of age 39(34.2%). These results showed similarities to the study conducted by Monalisa Jena *et al*[10].Table-4 shown presence of comorbidities in epileptic patients. Majority 85(74.6%) had no comorbiditieswhereas29(25.4%) were with comorbidities.

Overall AEDs utilization for the treatment of epileptic seizures shown in Table-5.AED Prescription Pattern shows Carbamazepine was the most frequently prescribed monotherapy was found in 14 cases(12.2%) prescriptions, followed by leviteracetam in 12 cases (10.5%). This observation was not in accordance with any of the previous studies. Phenytoin with phenobarbitone is the only drug combination found in the study. This study is in accordance with the study conducted byBadwaik RT *et al*[11].Table-6 showed AEDscategorization of antiepileptic drugs, that all epilepticpatients were managed with conventional AEDs 39 (34.2%) patients. This study is in accordance with the study conducted by WakjiraRishe*et al*[8].Adverse drug effects of antiepileptic drugs areobserved in epilepsy patients are found inTable-7 and headache 22(19.2%) was most common ADRs found.Similar observations were found in the study conducted by WakjiraRishe*et al* [8].Number of drug interactions present in AED prescriptions is shown inTable-8.Out of 114 prescriptions, 42 cases (36.8%) are reported potential drug interactions. All the previous studies reveal that the majority of drug regimen having possible drug interactions. Our studyresults revealedthat the drug interactions were less reported than previous studies.AED prescription patternis shown in Table -9, out of 114 cases,54 patients (47.3%) receivedmonotherapy which found more than other therapy. Similar study observations were also found in WakjiraRishe *et al* [8], Faizan Mazhar *et al*[9], Badwaik R.T *et al*[11].

AEDs use profile of the type of epileptic seizures is found in Table-10. From the results, out of 31 cases, simple partial seizure patients 8(25.8%) received monotherapy while 18(58.1%) received dual therapy, 4(12.9%) treated with triple therapy. This result showed similarities to the study conducted byFaizan Mazhar *et al*[9].

Table-11 shows that, overall utilization of various AEDs in different types of seizures. From the results, levetircetam was mostly prescribed drug 51(44.7%) and it was given for simple partial seizure 21(41.1%). Such an observation was not found in any of the previous studies. Sodium valproate 27 (23.6%)was third frequently prescribed drug and was given mostly for generalized tonic clonic seizure 10(37.0%). Similar study was found in the study conducted by K.S.G. Arulkumaran *et al* [12].For complex partial seizure, carbamazepine 8(26.6) was most frequently prescribed AED drug and this result has got similarities of studies conducted by K.S.G. Arulkumaran *et al* [12] and SwethaMunoli*et al* [13]. Phenytoin with phenobarbitone was the only combination found in our study and this result has also got similarities with the studies conducted by Badwaik RT *et al* [11]and Wakjira Rishe *et al* [8].

While checking for the presence of any contraindicated drugs, we have found that none of the patients medication chart had any contraindicated drugs being prescribed. Such similar observation was found in WakjiraRishe et al [8].

Table 1: Socio-demographic characteristics of patients with Antiepileptic drugs

Socio-demographicvariables			Number of patients	Percentage (%)
Gender	M	-	63	55.3
	F	-	51	44.7
	Total	-	114	100
Age (Years)	< 5	M	6	5.3
		F	5	4.4
	5 – 18	M	28	24.6
		F	12	10.5
	19 – 65	M	25	21.9
		F	28	24.6
	> 65	M	4	3.5
		F	6	5.3
	Total	-	114	100
Educational statusof patient	Illiterate	-	9	7.9
	Primary	-	22	19.3
	High School	-	25	21.9
	Higher Secondary	-	16	14.0
	Graduate	-	31	27.2
	NA	-	11	9.6
	Total	-	114	100
Family history	No	-	97	85.1
	Yes	-	17	14.9
	Total	-	114	100

(M - Male; F- Female; NA- Not Applicable)

Table 2: Classification of epileptic seizures

Classification ofseizures	Number ofpatients	Percentage (%)
Simple partial	31	27.2
Complex partial	27	23.7
Generalized absence	4	3.5
Generalized myoclonic	3	2.6
Generalized clonic	2	1.8
Generalized tonic	6	5.3
Generalized tonic clonic	26	22.8
Atonic	6	5.3
Status epilepticus	3	2.6
Febrile	3	2.6
Late onset seizure	3	2.6
Total	114	100

Table 3: Onset of initial epilepsy attack

Onset of initial epilepsy attack (Age in years)	Number of patients	Percentage (%)
< 5	39	34.2
5 – 18	33	28.9
19 – 65	38	33.3
> 65	4	3.5
Total	114	100

Table 4: Presence of Co- morbidities in epileptic patients

Co-morbidities	Frequency	Percentage (%)
Yes	29	25.4
No	85	74.6
Total	114	100

Table 5: Overall AEDs utilization for the treatment of epileptic seizures

AED drugs	AEDsprescription pattern			
	Mono therapy	Dual therapy	Triple therapy	Poly therapy
Carbamazepine	14	11	5	0
Levetiracetam	12	28	10	1
Phenytoin	10	6	2	0
Sodium valproate	4	18	4	1
Phenobarbitone	3	5	0	0
Clobazam	7	16	6	1
Oxcarbazepine	3	5	2	1
Lacosamide	1	8	6	0
Gabapentin	0	1	2	0
Lorazepam	0	1	0	0
Topiramate	0	2	0	0
Phenytoin+Phenobarbitone	0	0	0	1

Table 6: AEDscategorizationof antiepileptic drugs

AEDs categorization	Number of patients	Percentage (%)
Conventional AEDs	39	34.2
Newer AEDs	37	32.5
Conventional/Newer	38	33.3
Total	114	100

Table 7: Data of ADRs in epileptic patients

ADRs in Patients	Number of patients	Percentage (%)
Headache	22	19.2
Loss of appetite	9	7.8
Drowsiness	7	6.1
Insomnia	6	5.2
Sedation	5	4.3
Memory loss	3	42.6
Confusion	2	1.7
Myopathy	2	1.7
Hypersensitivity	2	1.7
Hair loss	1	0.8
Dizziness	1	0.8
Blurred vision	1	0.8
Vomiting	1	0.8
Nil	52	45.6
Total	114	100

Table 8: Number of potential drug interactions present in AEDsprescriptions

Potential drug Interaction	Number of patients	Percentage (%)
No	72	63.2
Yes	42	36.8
Total	114	100

Table 9: AED prescription pattern

ADRs categorization	Number of patients	Percentage (%)
Mono Therapy	54	47.3
Dual Therapy	42	36.8
Triple Therapy	17	14.9
Poly Therapy	01	0.8
Total	114	100

Table 10: AEDs use profile of the type of epileptic seizures

Types of epileptic seizures	AEDs Prescription Pattern				Total
	Mono therapy	Dual Therapy	Triple therapy	Poly therapy	
Simple partial (n)	8	18	4	1	31
Percentage (%)	25.8	58.1	12.9	3.2	100
Complex partial (n)	18	8	1	0	27
Percentage (%)	66.7	29.6	3.7	0	100
Generalized absence (n)	4	0	0	0	4
Percentage (%)	100	0	0	0	100
Generalized myoclonic (n)	1	1	1	0	3
Percentage (%)	33.3	33.3	33.3	0	100
Generalized clonic (n)	2	0	0	0	2
Percentage (%)	100	0	0	0	100
Generalized tonic (n)	4	1	1	0	6
Percentage (%)	66.7	16.7	16.7	0	100
Generalized tonic clonic (n)	9	13	4	0	26
Percentage (%)	34.6	50.0	15.4	0	100
Atonic (n)	2	3	0		5
Percentage (%)	40.0	60.0	0	0	100
Status epileptics (n)	1	2	0	0	3
Percentage (%)	33.3	66.7	0	0	100
Febrile (n)	2	1	0	0	3
Percentage (%)	66.7	33.3	0	0	100
Late onset seizure (n)	0	3	0	0	3
Percentage (%)	0	100	0	0	100

(n-in number; % - in percentage)

Table 11: Utilization of various AEDs in different type of seizures

Anti-Epileptic Drugs	Classification of Seizure's											No. of Patients	%
	Simple partial	Complex partial	Generalized absence	Generalized myoclonic	Generalized clonic	Generalized tonic	Generalized tonic-clonic	Atonic	Status epilepticus	Febrile	Late onset seizure		
LC	21	6	1	2	0	4	9	4	0	1	3	51	44.7
CB	15	8	2	0	0	0	3	0	2	0	0	30	26.3
CZ	6	5	0	2	1	2	11	1	2	0	0	30	26.3
SV	6	3	0	2	0	0	10	5	1	0	0	27	23.6
PH	0	5	0	1	1	0	8	1	0	2	0	18	15.7
LA	7	1	0	0	0	0	3	0	0	1	3	15	13.1
OX	0	3	1	0	0	3	2	2	0	0	0	11	9.6
PB	3	2	0	0	0	0	2	0	1	0	0	8	7.0
GP	2	1	0	0	0	0	0	0	0	0	0	3	2.6
TM	0	1	0	0	0	0	0	0	1	0	0	2	1.7
LZ	1	0	0	0	0	0	0	0	0	0	0	1	0.8
PP	1	0	0	0	0	0	0	0	0	0	0	1	0.8

LC-Levetriacetam; **CB** – Carbamazepine; **CZ** – Clobazam; **SV**- Sodium Valporate; **PH**- Phenytoin; **LA**– Lacosamide;**OX** – Oxcarbazepine; **PB**- Phenobarbitone; **GP**- Gabapentin; **TM**- Topiramate; **LZ**-Lorazepam; **PP**-Phenytoin+Phenobarbitone

5. Conclusion

The majority of epileptic patients were males 63 under the age group of 19-65 years. Majority of the patients had simple partial seizures followed by complex partial seizures.Majority initial attack found to be in less than 5 years of age 39 (34.2%) were with comorbidities. Carbamazepine was the most common monotherapy. Most commonly prescribed dual therapy drug is levetiractam followed by sodium valproate. Levetiracetam is most frequently prescribed drug and Lorazepam is least prescribed drug. Out of 114 patients, 39 (34.2%) were given with conventional AEDs, 37 (32.5%) received newer AEDs and 38 patients were treated with both conventional/newer AEDs. Headache was most commonly observed ADR and there were only 36.8% drug interactions present among all collected data's. In simple partial seizure, dual therapy was most widely used and in complex partial seizure, monotherapy was used, but in late onset seizure, dual therapy was most commonly used 3(100%). Polytherapy was used in simple partial seizures case thatis only 1 patient out of 114 patients. Pharmacist play vital part in the overall process of DUEbecause of their experience in the area of pharmaceutical care. From the results, we conclude that the data findings would help to evaluate anti-epileptic drugs usage with the hospital indicators and guide to both 'practitioners' and 'patients' for epilepsy care in general practice as well as whoever involved in the patient care.

6. Acknowledgements

7. Source of Support

Nil

8. Conflict of Interest

None

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