

Clinical assessment and comparative therapeutic evaluation of levetiracetam and its combinations (levetiracetam with lacosamide, levetiracetam with phenytoin, levetiracetam with sodium valproate) in epilepsy

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ABSTRACT

Background: Epilepsy is the second most common and frequently encountered neurological condition that imposes heavy burden on individuals, families and also on healthcare systems. The majority of patients with epilepsy become seizure free with levetiracetam in clinical practice.

The purpose of the study is to assess the efficacy and comparative therapeutic evaluation of levetiracetam and its combinations (Levetiracetam with lacosamide, levetiracetam with phenytoin, levetiracetam with sodium valproate).

Method: This is a prospective observational study conducted in SIMS hospital Narasaraopeta. A total of 150 sample population was included in our study who were on antiepileptic medication. In this we compare levetiracetam alone (i.e., monotherapy) with levetiracetam combinations to assess the efficacy and

safety drug profile from September 2021 - March 2022 i.e., period of 6 months.

Results: In 150 study population the patients who were using levetiracetam as monotherapy 24% (n=36) and the patients who are using other antiepileptics along with levetiracetam as combination therapy are 76% (n=14).

The efficacy of the therapy is assessed by measuring the episodes of seizures before the treatment and after the treatment. The ADRS that we observed in patients who are receiving only levetiracetam (n=36) is anger (n=10) and nausea (n=2) and the ADRS that are observed in patients who are

receiving levetiracetam and lacosamide (n=73) is anger (n=8), GI disturbances (n=5), dizziness (n=1), and the ADRS observed in patients who are receiving levetiracetam and phenytoin (n=2) is irritability (n=4), nausea (n=2), dizziness (n=3).

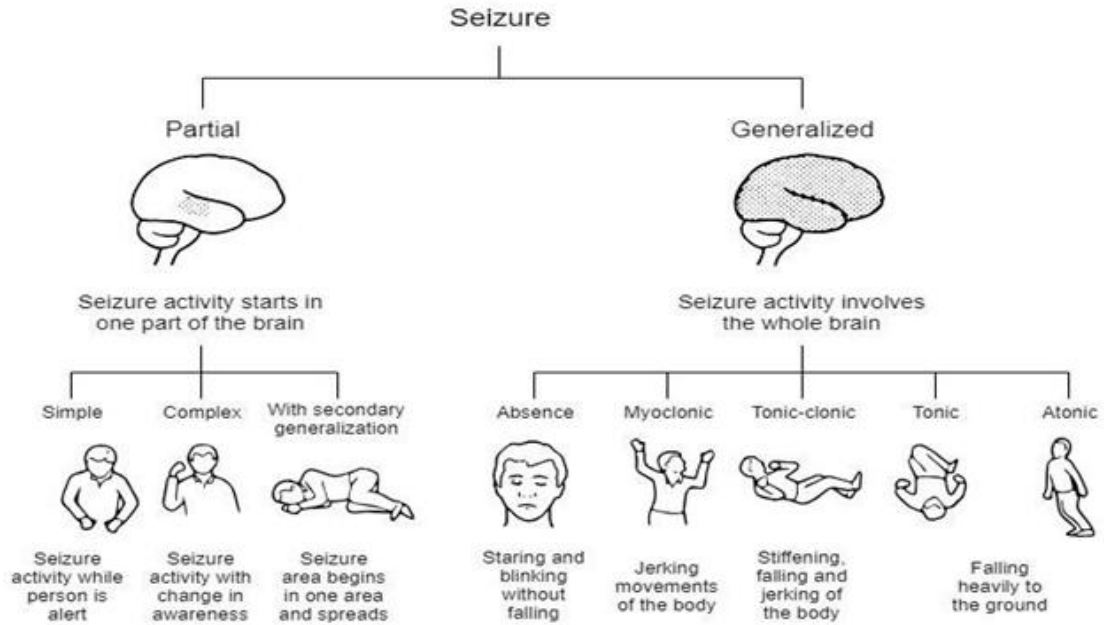
Conclusion: Based on our study we found that levetiracetam works more effectively and significantly reducing the number of seizures when compared to lacosamide as it shows some mild ADRs. Compared to other treatment groups levetiracetam with lacosamide shows better efficacy and having safety profile and compared to monotherapy, combination therapy shows better efficacy and having mild ADRs.

KEYWORDS: Antiepileptic, epilepsy, seizure, monotherapy, combination therapy.

I. INTRODUCTION

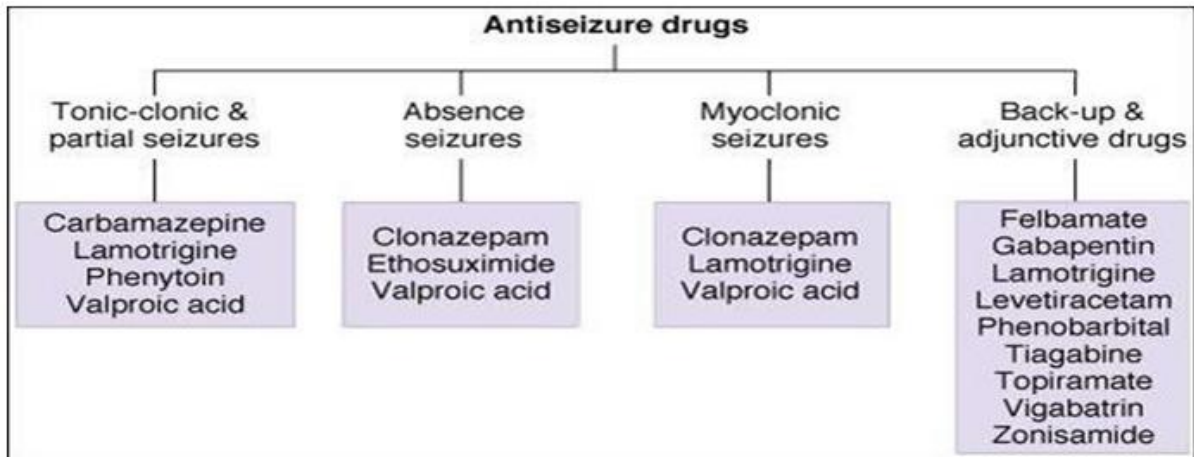
The word "epilepsy" has its origin in ancient Greek which means "to seize, possess, or afflict."⁽¹⁾ Epilepsy is a neurological disorder characterized by chronic predisposition marked by sudden recurrent episodes of sensory disturbance, loss of consciousness, or convulsions, associated with abnormal electrical activity in the brain, which require typically two unprovoked seizures. A seizure is defined as an abnormal, disorderly discharge of the brain's nerve cells, resulting in a temporary disturbance of motor, sensory, or mental function.⁽²⁾

Types of seizures:



PHARMACOLOGICAL THERAPY:

The ultimate goal of treatment for epilepsy is to control seizures and to have no side effects with an optimal quality of life. The best quality of life is associated with seizure-free state.



II. MATERIALS AND METHODS

• Study Site:

This study was conducted at the SIMS Hospital in Narasaraopet.

• Study Period:

A period of 6 months (October 2021–March 2022)

• Sample Size:

A total of 150 patients from the In-patient of the Department of neurology those who fulfilled the inclusion and exclusion criteria were selected for the study.

• Study Criteria:

Inclusion Criteria:

1. The study population must be between the age group of above 18 years
2. The patients must stay in the hospital for more than 24 hours.
3. Patients having at least one episode of seizures.

Exclusion Criteria:

1. Patients below the age of 18 years.
2. Outpatients should not be taken into the account.
3. Pregnant women are excluded. Patients having comorbidities are excluded.

Source of data:

The patient's demographical data, clinical data, therapeutics data and various other relevant and necessary data were obtained every day from the medical records and other relevant information sources are documented.

a. RESULTS

Table 01: Distribution of Study Population

Type of population	Sample size	Percentage (%)
Patients using Levetiracetam (monotherapy)	36	24
Patients using other AEDS along with LVT (combinational therapy)	114	76
Total	150	100

Table 1: Patients using Levetiracetam as monotherapy are 24% and patients using other anti-epileptic drugs along with Levetiracetam as combinational therapy are 76%.

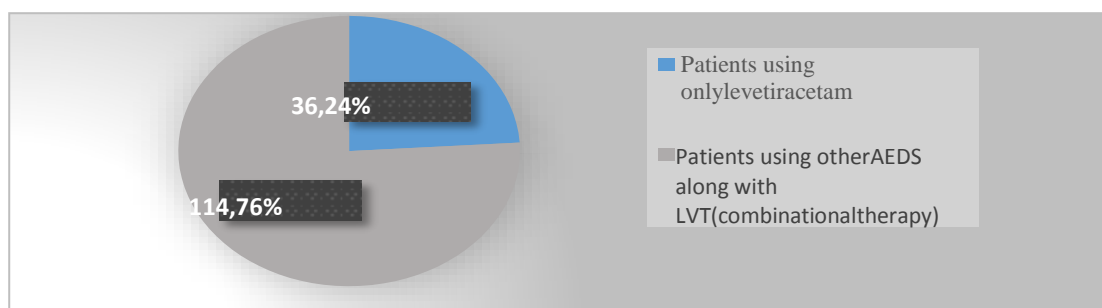


Figure 1: Distribution of study population

Table 02: Age wise distribution of study population:

Age group	Diseased population	Percentage (%)
19–27	19	12.6
28–37	35	23.3
38–45	28	18.6

46-56	27	18
57-67	21	14
>68	20	13.3
Total	150	100

Table 2: Majority of the population fall between age group of 28-37 i.e., 35 (23.3%) followed by 38-45 years i.e., 28(18.6%) and the least was found in 19-27 years i.e., 19(12.6%).

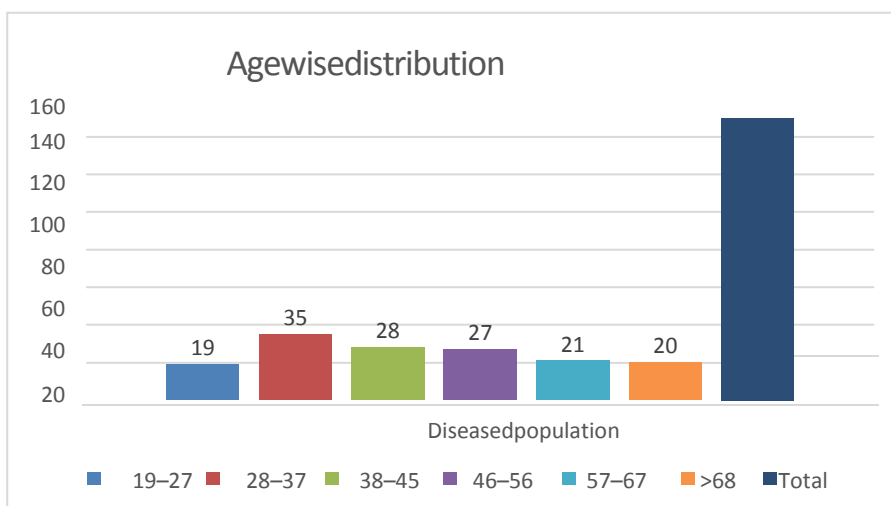


Figure2: AgeWiseDistributionofstudypopulation

Table-03: Genderwisedistributionofstudypopulation:

Gender	Diseasedpopulation	Percentage(%)
Male	85	56.6
Female	65	43.3
Total	150	100

Table:03 Majority of participants were included as males in population group i.e., 56.6% (85) females included in this study are 43.3% (65).

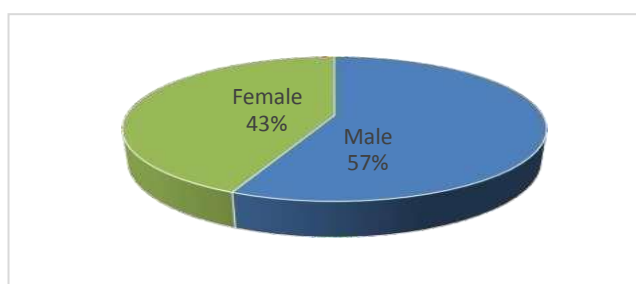


Figure 3: Gender Wise Distribution of Study Population

Table-4: Distribution of diseased population based on type of epilepsy:

Type	No.Ofpatients	Percentage(%)
Febrileseizures	10	6.6
Myoclonicseizures	23	15.3
Partialeizures	25	16.6
Focalseizures	23	15.3
Absenceseizures	27	18
Generalisedtonicclonic seizures	42	28
Total	150	100

Table:4 Generalized tonic clonic seizures were the predominant seizure type, encountered about 28% (42), followed by myoclonic seizures 15.3% (23), partial seizures 16.6% (25), focal seizures 15.3% (23), absence seizures 17% (17), febrile seizures 6.6% (10).

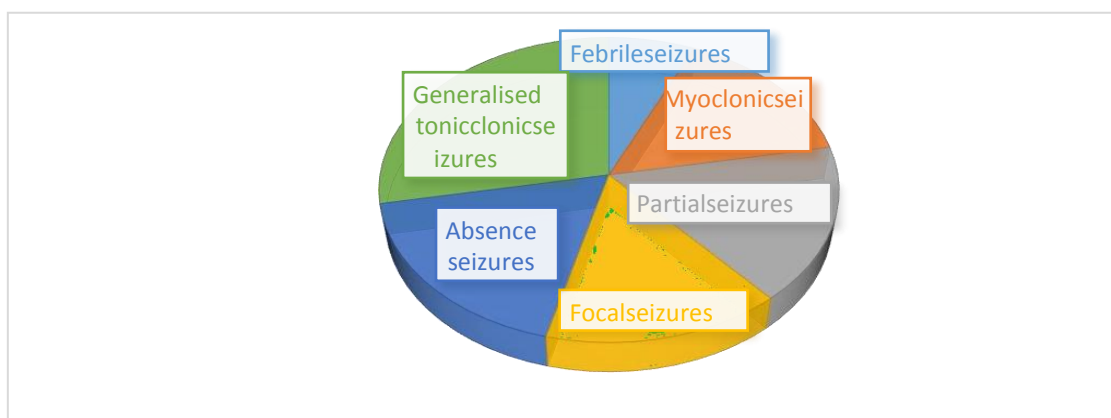


Figure-4: Distribution of diseased population based on type of epilepsy

Table-5: Distribution of patients based on AED therapy:

S.no	Treatment groups	No.ofpatients prescribed	Percentage(%)
1	Levetiracetam	36	24
2	Levetiracetam+lacosamide	73	48.6
3	Levetiracetam+phenytoin	21	14
4	Levetiracetam+sodiumvalproate	20	13.3
5	Total	150	100

Table:5 Patients using only levetiracetam (n=36) and the patients using LVT along with lacosamide (73), patients using LVT with Sodium valproate (20), and the patients using LVT with phenytoin (21).

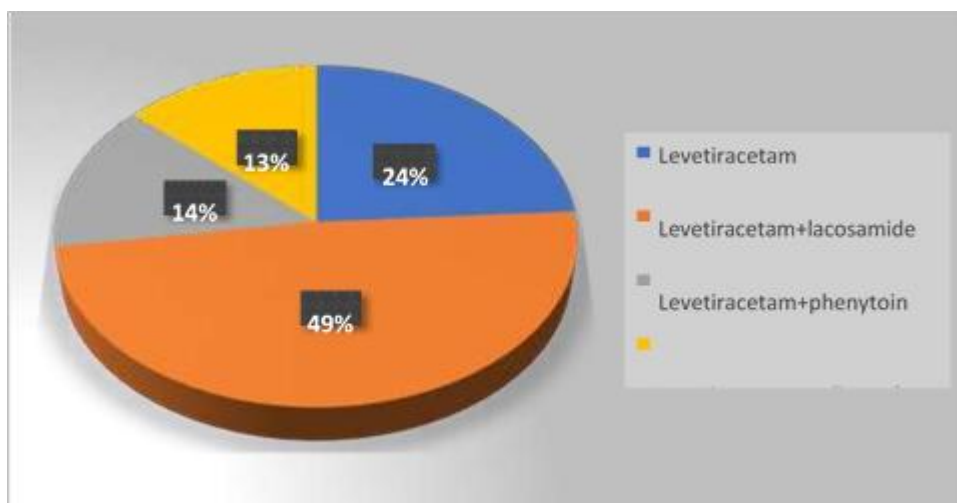


Figure-5: Distribution of patients based on AED therapy

Table 6: Assessment of efficacy of levetiracetam (LVT) alone and LVT with other AED's

BEFORE TREATMENT

S.no	Parameters	LVT	LVT + Lacosamide	LVT+ Phenytoin	LVT + sodium valproate
1.	No. of patients having one episode of seizures	14 (38.8%)	37 (50.6%)	9 (42.8%)	11 (55%)
2.	No. of patients having two episodes of seizures	17 (47.2%)	25 (34.1%)	10 (47.6%)	6 (30%)
3.	No. of patients having three episode of seizures	5 (13.8%)	11 (15%)	2 (9.5%)	3 (15%)

AFTER TREATMENT

S.no	Parameters	LVT	LVT with Lacosamide	LVT with Phenytoin	LVT with Sodium valproate
1.	No. of patients having one episode of seizures	5 (13.8%)	10 (13.6%)	3 (14.2%)	5 (25%)
2.	No. of patients having two episodes of seizures	6 (16.6%)	4 (5.4%)	2 (9.5%)	2 (10%)
3.	No. of patients having three episode of seizures	1 (2.7%)	0	0	0

Table: 6 After assessing before and after treatment, before treatment patients having one

episode, two episodes, three episodes of seizures are reduced after usage of treatment

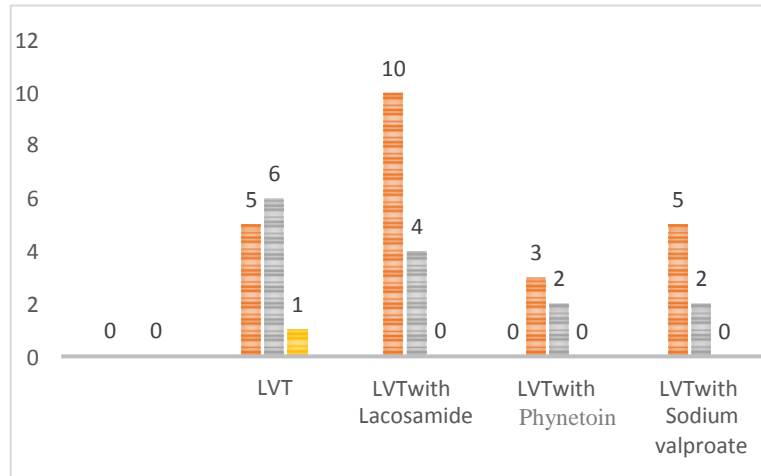


Table 11: Safety profile of different combinations of anti-epileptics prescribed:

Type of reaction	Levetiracetam (n=36)	Levetiracetam + lacosamide (n=73)	Levetiracetam + phenytoin (n=21)	Levetiracetam + Sodium valproate (n=20)
Anger	10 (27.7%)	8 (10.9%)	-	1 (5%)
Irritability	-	-	4 (19%)	
GI disturbance	-	5 (6.8%)	-	3 (15%)
Nausea	2 (5.5%)	-	2 (9.5%)	2 (10%)
Dizziness	-		3 (14.2%)	2 (10%)

Table 11: In overall study period, the maximum number of ADRs experienced in patients using levetiracetam with phenytoin are irritability (19%), nausea (9.5%) dizziness (14.2%) and the least ADRs was found in patients using levetiracetam with lacosamide are anger (10.9%), GI disturbances (6.8%).

IV DISCUSSION:

In 150 study population the patients who are using levetiracetam as monotherapy 24% (36) and the patients who are using other Antiepileptic's along with levetiracetam as combinational therapy are 76% (114). In this study a total of 23.3% (35) were in the age group of 28-37 followed by 38-45 years

i.e., 18.6% (28) and the least was found in 19-27 years i.e., 19 (12.6%).

In our study we observed that the prevalence of epilepsy is more common in men than women. From our study we had the data on individual risk factors for epilepsy. Among 150 epileptic patients the major risk factors we observe are age i.e., 38% followed by idiopathic 28% (42), genetics 18.6% (28), trauma 8.6% (13), and fever 6.6% (10). In our study the generalized tonic-clonic seizures were the predominant seizure type, encountered about 28% (42), followed by myoclonic seizures 15.3% (23), partial seizures 16.6% (25), focal seizures 15.3% (23), a

absence seizures 17% (17), and the least was found to be focal seizures 6.6% (10).

In 150 diseased population the patients using levetiracetam is 24% (n=36). The patients that are using combination therapy i.e. levetiracetam and lacosamide is 48.6% (n=73) and the patients using levetiracetam and phenytoin is 14% (n=21) and patients using levetiracetam and sodium valproate is 13.3% (n=20).

Regarding the assessment of efficacy of levetiracetam with lacosamide it shows more efficacy in patients with two episodes of seizures. Regarding the assessment of efficacy of levetiracetam with phenytoin, it shows more efficacy in patients with two episodes of seizures. Regarding the assessment of efficacy of levetiracetam with sodium valproate, it shows more efficacy in patients with one episode of seizures.

In our study the safety profile of AED was assessed by observing the ADRs. Based on this we observed that patients using levetiracetam and lacosamide having less side effects compared to other AEDs.

V. CONCLUSION

In our study population, the patients who are using levetiracetam as monotherapy were 24% & patients using combination therapy were 76%.

We divided the population based on treatment groups & assessed the efficacy of treatment groups based on seizure reduction. In our study we included pharmacovigilance aspects of different treatment groups, it is observed that patients using levetiracetam and lacosamide combination having less side effects when compared to other antiepileptic combinations as well as monotherapy.

The results in our study signify that combination therapy shows better efficacy than monotherapy. Levetiracetam and lacosamide combination shows better efficacy and having safety profile compared to other antiepileptic combinations.

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