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COMPARATIVE STUDY OF EFFICACY AND SAFETY OF LEVETIRACETAM AND CARBAMAZEPINE AS MONOTHERAPY IN PARTIAL SEIZURES

Pharmacology

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ABSTRACT

Background: Carbamazepin is the preferred drug while levetiracetam is a newer drug for partial seizures. In this study, efficacy and safety of levetiracetam and carbamazepine as monotherapy in partial epilepsy is compared.

Methods: Patients were randomized in two groups. Group LEV (n=30) participants were prescribed Tab Levetiracetam, 1000–3000 mg/day/oral; and group CBZ (n=30) participants were prescribed Tab Carbamazepine, 400–1200mg/day/oral. Seizure freedom, adverse effects, quality of life was assessed at the end of 12 weeks.

Results: No statistical significant difference ($p > 0.05$) in both groups in seizure free interval (96.67% vs. 80%) and number of adverse effect (30% vs. 33.33%). Improvement in quality of life was better in group LEV (64.50%) than group CBZ (57.13%) which is statistically significant.

Conclusion: Efficacy and safety of levetiracetam is comparable to carbamazepine in partial seizure while quality of life is better with levetiracetam.

KEYWORDS

Quality of life, Seizure free interval, Epilepsy

INTRODUCTION

Epilepsy is a common but serious brain disorder. It is universal, with no age, sex, geographical, social class or racial boundaries. Epilepsy imposes a large economic burden on health care systems of countries. There is also a hidden burden associated with stigma and discrimination against the patients and even their family in the community, workplace, school and home. Many patients with epilepsy suffer severe emotional distress, behavioural disorders and extreme social isolation. Thus, the Regional Office for South-East Asia (SEARO) of the World Health Organization (WHO) has decided to give high priority to the control of epilepsy in the community.[1]

The word "epilepsy" is derived from Latin and Greek words for "seizure" or "to seize upon".[2] Epilepsy can be defined as "the occurrence of transient paroxysms of excessive or uncontrolled discharges of neurons, which may be due to a number of different causes leading to epileptic seizures". The actual presentation or manifestation differs among individuals, depending upon the location of the origin of the epileptic discharges in the brain and their spread.[1]

World Health Organization (WHO) and International League against Epilepsy (ILAE) have estimated that, out of 50 million people, 34 million with epilepsy live in developing countries. Out of them, nearly 80% are not on treatment.[2] In India, it is estimated that, out of over 1.23 billion population, there are around 6–10 million people with epilepsy. It accounts for nearly 1/5th of global epilepsy burden.[3]

Epilepsy is classified based on the source of seizure into partial and generalized seizures. Partial (focal) seizures arise in specific, often small, loci of cortex in one hemisphere of the brain. They are divided into simple partial seizures, which occur without alteration of consciousness and complex partial seizures in which consciousness is impaired or lost. About 2/3rd of newly diagnosed epilepsies are partial or secondarily generalized. The treatment of the epilepsy depends on appropriate classification of seizure type and the epileptic syndrome.[4] Carbamazepine (CBZ) is the preferred drug for the treatment of partial seizures but has the disadvantages of requirement for frequent dosing, dose related adverse reactions and drug interactions. Recently, Levetiracetam (LEV) has become one of the most frequently prescribed newer drugs for the treatment of partial seizures. It offers several advantages like twice daily dosing, better safety profile, less drug interactions and no requirements of serum level monitoring. This advantageous pharmacologic profile makes LEV as an attractive first line or adjunctive therapy for epileptic seizures.[5]

Till date, there have been a very few studies on the efficacy and safety of LEV and CBZ in partial epilepsy. Hence, this study is undertaken to compare the efficacy and safety of levetiracetam and carbamazepine as monotherapy in partial epilepsy.

MATERIAL AND METHODS

The study was conducted in a tertiary care hospital attached to a medical teaching institute in central India, after being approved by Institutional Ethics Committee. This was prospective, comparative, randomized, open labeled study. Patient recruitment was done from January 2017 to May 2018. All the patients coming to medicine department outpatient and inpatient were considered for recruitment. Patients willing to participate in study were screened for inclusion and exclusion criteria. All newly diagnosed patients of partial seizures and all patients with intracranial haemorrhage, trauma, brain infection, liver or kidney failure, very high blood pressure, use of illegal drugs, Cerebrovascular accidents presented with partial seizures of either gender between age group 18 to 60 years were included in study. Patients with other types of seizures, pregnant and lactating mothers were excluded from study. The participants were included in the study after obtaining written informed consent. The patients were allocated to either Group LEV or Group CBZ of the treatment based on simple random sampling (Chit-Pull method).

Group LEV participants were prescribed Tab LEV, 1000–3000 mg/day/oral; and Group CBZ participants were prescribed Tab CBZ, 400–1200mg/day/oral. The participants were started with minimum dose, 500mg of LEV and 200mg of CBZ, given twice daily after food and then titrated depending on the seizure control. LEV dose was increased by 500 mg twice daily every 2 weeks up to a maximum of 3000mg/day if seizure control was not achieved. Similarly, CBZ dose was increased by 200mg twice daily up to a maximum of 1200mg/day if seizure control was not achieved. In cases where the seizure was not controlled after titration of drug dose, the participant was shifted to adjuvant therapy based on the clinical condition. The participant was also discontinued from the study. All the participants were given a drug diary and were asked to note down any adverse event (AE). They were advised to come after 4 and 12 weeks after the initiation of therapy for follow-up. During follow-up visits, the participants were thoroughly examined, history of breakthrough seizures was elicited, and any AEs were noted. Quality Of Life (QOL) was assessed by using the QOLIE-10 (Quality Of Life In Epilepsy) questionnaire before initiation of the treatment and after 12 weeks of therapy. The English version of QOLIE-10 was used for this study. Participants who were conversant

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in English completed the questionnaire themselves. Since the remaining patient population was multilingual (Kannada, Hindi, Bengali, and Telugu), the questions were explained to them in their respective languages and responses were elicited. The responses were then scored to provide subscale scores which were then averaged to provide a total score. Unpaired t test was used to compare demographic characteristic, seizure freedom, and QOL score while z test was used to compare age and adverse event in two treatment group. $P < 0.05$ is considered statistically significant.

OBSERVATIONS AND RESULTS

A total 270 patients were screened for the study, 74 patients fulfilled inclusion-exclusion criteria. Out of which 62 were consented to participant in study, of which 31 patients were allocated to Group LEV and 31 patients to Group CBZ. During the study period, one patient from each group lost to follow up. Thus, 30 patients from each group completed the study and were considered for the analysis of data.

All the patients maintained drug diary properly. Demographic characteristic of two treatment group is shown in table 1. Table 2 shows seizure freedom in two treatment group at the end of 4 weeks and 12 weeks. Adverse events occurred during study period are mentioned in table 4. QOLIE-10 questionnaire average score is displayed in table 4.

Table 1: Demographic characteristic of two treatment groups

Variables	Group LEV (n=30)	Group CBZ (n=30)	P VALUE
Age (years) (Mean ± SD)	30.70 ± 2.66	22.62 ± 1.152	>0.05#
Male	19	21	>0.05**
Female	11	9	>0.05**

unpaired t test, ** Z test, SD = Standard Deviation

Table 2: seizure freedom in two treatment groups

Seizure freedom	Group LEV (n=30) (%)	Group CBZ (n=30) (%)	P VALUE#
4 week	90.00	73.33	>0.05
12 week	96.67	80.00	>0.05

unpaired t test

Table 3: Adverse eevents in two treatment groups

Adverse Events	Group LEV		Group CBZ		P value**
	No. of patients	%	No. of patients	%	
Dizziness, ataxia, fatigue	01	03.33	02	06.67	>0.05
Weight gain	01	03.33	03	10.00	>0.05
Behavioural symptoms	04	13.33	01	03.33	>0.05
Nausea/ vomiting	03	10.00	04	13.33	>0.05
Total	09	30.00	10	33.33	>0.05

**Z test for difference between two proportion

Table 4: QOLIE-10 questionnaire score in two treatment groups

Duration	Group LEV	Group CBZ	P value#
0 week	27.93±01.17	30.60±01.30	>0.05
4 week	51.73±01.38	41.70±01.41	<0.05
12 week	64.50±01.83	57.13±01.35	<0.05

unpaired t test, values are expressed as Mean ± SD

DISCUSSION

In the present study, the primary outcome was seizure freedom with both the monotherapy at the end of 12 weeks. Seizure freedom at the end of 12 weeks was 96.67% and 80.00% in group LEV and group CBZ respectively. The difference between two groups is not statistically significant. In accordance with our study, Suresh SH et al[6] and Perry et al[7] reported same results. At the end of 12 weeks, group CBZ showed more adverse effects than LEV though the difference is not statistically significant. Similarly, Suresh SH et al[6] and Perry et al[7] reported no statistically significant difference between two groups while in contrast to our study Pohlmann-Eden et al[8] reported more adverse events with Levetiracetam therapy. At the end of both 4 weeks and 12 weeks group LVZ showed more improvement than group CBZ in quality of life which was statistically significant. Similar results are reported by Suresh SH et al[6] and Perry et al[7].

Single centred, open label study with small sample size and short duration are some of the limitations of study.

CONCLUSION

Monotherapy levetiracetam is compararble to monotherapy carbamazepine in partial seizure patients in veiwe of seizure free interval and adverse events while better than monotherapy carbamazepine in improving quality of life. Levetiraetam can be considered as better option for treatment of partial seizures.

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