Original Article

Efficacy and Tolerabilityof Leviteracetum and Topiramate in Patients with Epilepsy

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Abstract

A total of 50 patients were enrolled for study purpose. The study conducted was a prospective, observational study from July 2009 to October 2009. Patients were seen on five separate occasions (1) Baseline (week 0) At the beginning of initial treatment, patients were divided into two groups i.e; Topiramate gp; and Levetiracetam. Patients were given the respective drugs and then asked to follow up after fifteen days. First follow-up visit was after 15 days of treatment, second follow-up visit (30 days after first follow-up visit, third follow-up (after 45 days) and final visit (60 days after initial treatment). Levetiracetam was administered at a dose of 250 – 500 mg b. i. d and Topiramate 50 mg b i d. During each phase concomitant anti-epileptic regimes remained constant. In addition Folic acid was prescribed to every patient. Statistical analysis was performed using software SPSS version v. 16.0 for Windows. In the primary analysis 95% confidence intervals for both upper and lower bound means, ANOVA and t-test were performed.

Conclusion: This study supports the effectiveness of Anti-Epileptic Drugs as add – on therapy. Topiramate did not prove superior, but it may be a good choice for patients allergic to other anti-epileptic drugs because of the lower risk for rash. Levetiracetam is a broad-spectrum AED and compares well with long – acting VPA and CBZ. Results may have been better with an Extended Release (ER) formulation of Levetiracetam. The retention rate for LEV is statistically significant as is TPM. LEV had a more favorable side effect profile than TPM with comparable efficacy. Patients on TPM discontinued treatment mainly because of neurocognitive side effects and allergic reactions. In the treatment

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with LEV, the effects on mood must not be underestimated.

Keywords: Epilepsy, seizures, antiepileptic drugs, levetiracetam, topiramate.

Introduction

The term 'epilepsy' embraces a constellation of seizures and syndromes, each manifest by recurrent epileptic seizures resulting from abnormal, excessive or hypersynchronous neuronal activity. Approximately 50 million people suffer from this disorder worldwide with nearly 90% being in developing countries[1.] The disorder is usually controlled, but not cured, with medication. However, 30% of people with epilepsy do not have seizure control even with the best available medications.[2,3] The last decade has seen the development of ten new anti-epileptic drugs. The shared heterocyclic ring structure in older anti epileptics may underlie the allergic reactions in some patients to more than one drug. Structures of the newer drugs possess fewer similarities to the older agents and to each other reflecting perhaps unique mechanisms of drug interaction.[4] Levetiracetum (LEV) is a new anti-epileptic drug that is clinically effective in generalized and partial epilepsy syndromes. Leviteracetum binds to a synaptic vesicle protein, SV2A.[7] This is believed to impede nerve conduction across synapses.[8]

It modulates seizure – activity in a dichotomous fashion, a possible explanation for which is that LEV has different mechanisms of action, whether given acutely or chronically and in 'epileptic' and control tissue.[5,6] Leviteracetum has recently been approved in the United Kingdom as a monotherapy treatment for epilepsy. It is also used in veterinary medicine for similar purposes.[9]

Topiramate treats epilepsy in children and adults. It is sometimes used as a mood stabilizer.[13] In children it is indicated for the treatment of Lennox – Gastaut syndrome, a disorder that causes seizures and developmental delay.[10] Topiramate has a complex mechanism of action[11] the drug enhances GABA – activated chloride channels. In addition, it inhibits excitatory neurotransmission. Its possible effect as a mood stabilizer seems to occur before anticonvulsant qualities at lower dosages.[12] In light of these emerging facts, we sought to determine the efficacy and tolerability of leviteracetum and topiramate in patients with epilepsy and the effect of these drugs in providing enhanced seizure control in the out – patient population.

Methodology

A total of 50 patients were enrolled for study purpose. The study conducted was prospective and observational, from July 2009 to October 2009. It was conducted in three distinct phases: Phase (0) baseline, Phase (1) baseline 15 days without add on therapy, Phase (2) 15 days with add-on therapy with Levetiracetam and Topiramate in combination therapy with carbamazapine (CBZ) and / or valproic acid (VPA), (3) follow up phase; follow-up assessment of seizure free days (SFD) Seizure count was obtained from the patient feedback from provided in the baseline phase.

Levetiracetam was administered at a dose of 250 – 500 mg twice a day and Topiramate 50 twice a day. During each phase concomitant anti-epileptic regimes remained constant. In addition Folic Acid was prescribed to every patient. Patients were seen on five separate occasion (1) baseline week 0 at the beginning of initial treatment, patients were then divided into two groups i.e; Topiramate gp; and Levetiracetam gp (LEV gp.); patients were given respective drugs and then asked to follow up after fifteen days. First follow-up visit, after 15 days of treatment, second follow-up visit (30 days after first follow-up visit, third follow-up (after 45 days), final visit (60 days after initial treatment).

Data was collected on age, gender, marital status, literacy level, occupation, seizure semiology, other anti-epileptic drugs used concomitantly with LEV or Topiramate, changes in seizure frequency and any adverse effects. An encouraging response to treatment was determined by a pronounced reduction (>50%) in seizure frequency **(seizure control).**

Results

50 patients were selected to participate in this study. 30 were males and 20 were females. 37 (74%) patients were diagnosed as Tonic clonic, whereas 4 (8%) were primarily diagnosed as Complex partial, 3 (6%) as tonic, 1 (2%) atonic and 1 (2%) as clonic (Table 1).

The patients were divided into two groups. One group was treated with Topiramate and the other with Levetiracetam (LEV). The frequency of seizures was observed per 15 days. At the first follow up 1 (2%) was with very good seizure control, 13 (46%) with good, 7 (14%) with adequate, 23 (46%) with poor and 6 (12%) were with very poor seizure control. Maximum seizures recorded within 15 days before starting

the treatment were 35, average seizures 3.08 ± 7.36 SD (Table 2).

Table 1: Types of Epilepsy.

Type of Epilepsy	Frequency	% age
Complex Partial	4	8.0
Primary Generalized (Absence)	4	8.0
Primary Generalized (Myoclonic)	1	2.0
Primary Generalized (Tonic)	3	6.0
Primary Generalized (Clonic)	1	2.0
Primary Generalized (Tonic Clonic)	37	74.0
Total	50	100.0

Table 2: Seizure Control At the start of study.

	Frequency	Percent
Very Good (no seizures)	1	2.0
Good (1 – 4)	13	26.0
Adequate (4 – 10)	7	14.0
Poor (upto 10)	23	46.0
Very Poor (> 10)	6	12.0
Total	50	100.0

At base line, average number of seizures in the Topiramate group was 1.85 ± 4.56SD (-0.28*-3.98, 95% C.I) maximum seizure count was 15, whereas in the Levetiracetam group the average number of seizures was 3.90 ± 8.73 (0.64 – 7.16, 95% C.I) and maximum seizure count was 35. The significance of seizure control is discussed in table 3.

Discussion

The purpose of our study was to determine seizure control in patients receiving Topiramate and Levetiracetum (LEV) as add on therapy. The study showed that both the drugs were equivalent in controlling seizures in either group as evident from table 2 and table 3. This observation coincides with the ones found in different studies[5,10] and.[11]

It is worthwhile to mention that for a number of patients continuing with Topiramate was difficult as it caused multiple allergic reactions and other adverse effects. Patients with LEV group tolerated the drug well with fewer side effects. The data was collected in the form of a questionnaire in which demographics including age, gender, marital status, literacy level, occupation, seizure semiology, other anti-epileptic drugs used concomitantly with LEV or Topiramate, changes in seizure frequency and any adverse effects were reported.

After evaluation of the questionnaires it was stipulated that the first occurrence of seizures for patients with epilepsy was highest for patients in the age range of 10 – 19 years with the next most prevalent age group being 0 – 9 years. Hence the onset of the seizures was found to be observed in young children and those in early adulthood.

One reason for the high illiteracy rate in this population the fact that this disorder is a limiting factor on the mental ability of the individual to excel in academic studies. The high unemployment rate is due to the same reasoning and their inability to fully participate in practical every day – to – day activities which includes employment. This is common for epileptic patients as they are suffering from mental depression caused by the anguish of not being recognized or employed by potential employers. Poor seizure control is accounted

Table3: Comparison of Topiramate and Levetiracetam groups in seizure control.

Drugs	Baseline	After 15 days	2nd follow up	3rd follow up	4th follow up
Topiramate Group	1.85 ± 4.56	0.21 ± 0.80	0.29 ± 0.61	0.15 ± 0.35	Nil
Levetiracetam Group	3.9 ± 8.73	0.21 ± 0.92	0.4 ± 0.94	0.11 ± 0.46	Nil
Statistics	Significant (P<0.05)	Non-significant (P >0.05)	Non-significant (P >0.05)	Non-significant (P >0.05)	Non-significant (P >0.05)

for by the fact that many of the patients were unable to continue with the time consuming treatment required for continuous therapy.

Conclusion

This study supports the effectiveness of AEDs as add-on therapy by itself, Topiramate did not prove superior, but it may be a good choice for patients allergic to other anti-epileptic drugs because of the lower risk for rash. Levetiracetam is a broad – spectrum AED and compares well with long-acting VPA and CBZ. Results may have been better with an Extended Release (ER) formulation of levetiracetam. The retention rate for LEV is significant as is TPM. LEV had a more favorable side effect profile than TPM with comparable efficacy. Patients on TPM discontinued treatment mainly because of neuro-cognitive side effects and allergic reactions. In the treatment with LEV, the effects on mood must not be underestimated.

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