JCEI /
Journal of Clinical and Experimental Investigations

2012; 3 (1): 108-110
doi: 10.5799/ahinjs.01.2012.01.0123

CASE REPORT

Essential tremor responsive to levetiracetam

Levetirasetama cevap veren esansiyel tremor

Aysel Milanlıoğlu[1], Ömer Faruk Odabaş[2], Abdullah Yılgör[3]

[1]Department of Neurology, Bitlis State Hospital, Bitlis, Turkey
[2]Department of Neurology, Konya Ereğli State Hospital, Konya, Turkey
[3]Department of Neurology, Yüzüncü Yıl University, Faculty of Medicine, Van, Turkey

ABSTRACT

Essential tremor is one of the most common movement disorders with a prevalence of 0.4% to 3.9% in the general population and increases with age. The medical treatment available for patients with essential tremor is often inadequate. Propranolol and primidone are the first-line treatment options, improving in up to two thirds of cases. This article reports a satisfying response to levetiracetam with disabling essential tremor in a 58-year-old man whom propranolol as well as primidone had to be discontinued due to unresponsiveness and severe side effects. One of the antiepileptic drugs, levetiracetam, may be more useful in the treatment of essential tremor. *J Clin Exp Invest 2012; 3(1): 108-110*

Key words: Essential tremor, anticonvulsant drug, levetiracetam

ÖZET

Esansiyel tremor, genel popülasyonda prevelansı % 0.4-3.9 olan ve yaş ile artan en sık görülen hareket bozukluğudur. Esansiyel tremorlu hastaların medikal tedavileri sıklıkla yetersizdir. Propranolol ve primidon vakaların 2/3'de ilk tercih tedavilerdir. Bu yazı, propranolol ve primidonu yanıtsızlık ve yan etkiler nedeni ile kesilen levetirasetama iyi cevap veren sakatlayıcı esansiyel tremorlu 58 yaşındaki bir erkek hastayı rapor etmektedir.

Antiepileptik ilaçlardan biri olan levetirasetam, esansiyel tremor tedavisinde daha fazla yararlı olabilmektedir.

Anahtar kelimeler: Esansiyel tremor, antikonvülzan ilaç, levetirasetam

INTRODUCTION

Essential tremor (ET) is one of the most common late-life movement disorder characterized by progressive postural and kinetic tremor typically affecting the hands, arms, head, voice, truck and leg.[1] Propranolol and primidone are the first-line treatment options. However, these drugs are ineffective in approximately 25–55 % of ET patients and are often have severe and potentially threatening adverse effects especially in elderly.

It is important to know the reality that no drug is yet available to eliminate tremor nevermore additional safe and well-tolerated drugs for the treatment of ET patients are promptly needed.[2] This article displays a case of ET who is effectively treated with levetiracetam (LEV).

CASE

A 58-year-old right-handed man referred to the outpatient clinic with a history of bilateral postural and kinetic tremor, which was first noted more than five years ago and developed gradually deterioration over the years. There was no drug use, family history or condition causing this movement disorder. The state of cerebellar signs or symptoms, hyperthyroidism, alcoholism, peripheral neuropathy and anxiety were ruled out and diagnosed definite ET. In his medical history, he had hypertension and diabetes. Brain magnetic resonance imaging showed diffuse cerebral atrophy and mild periventricular leuko-araiosis.

He was having difficulties in everyday activities like drinking, eating, dressing, writing, and other tasks requiring hand movements. Tremor severity was measured by using the Fahn-Tolosa-Marin clinical rating scale and scored as 3 points (markedly) at the first clinical examination.[3]

Medication was started with propranolol, first with daily dosage of 40 mg/day and increased gradually to 120 mg/day within four weeks. After three

Correspondence: Dr. Aysel Milanlıoğlu
Bitlis State Hospital, Department of Neurology, Bitlis, Turkey Email: ayselmilanlioglu@yahoo.com
Received: 08.04.2011, Accepted: 17.07.2011

months follow-up, any improvement was acquired and even gradually worsened, finally added primidone 250 mg/day, but it had to be discontinued because of the severe and threatening side effects like drowsiness, vertigo and unstable gait. After the ineffective and unwell-tolerated treatment options with propranolol and primidone, LEV was started and tolerated well, so the dosage was titrated from 500 mg/day to 2000 mg/day within four weeks. Six months follow-up, it showed a continuing ameliorating effect on ET, providing comfort for making simple activities of daily living. Moreover the repeat of Fahn-Tolosa-Marin clinical rating scale was scored as 2 points (moderately abnormal) and no functional disabilities were reported anymore.

DISCUSSION

Antiepileptic drugs are extensively used to treat a wide range of neurological disorders than epilepsy, such as neuropathic pain, migraine and ET.[4]

Recently, various agents including topiramate, benzodiazepines, gabapentin, zonisamide and levetiracetam that dramatically improve functions in ET patients have been documented in several trials.[5] In this case of 58-year-old man with ET, after inefficient and unwell-tolerated treatment with propranolol and primidone, LEV was found to be very effective. Additionally, the score of decline on Fahn-Tolosa-Marin clinical rating scale during the course of ET treatment with LEV also proved the efficiency. We observed antitremor effect in our patient after taking 1000 mg/day so the dosage was gradually titrated to 2000 mg/day for the significant effect. In literature, the maximum dose of LEV was 3000 mg/day which was reached by patients who did not benefit from lower doses after one week treatment with 1000 mg and four weeks treatment with 2000 mg/day.[6]

Levetiracetam is originally used as a broad-spectrum antiepileptic drug. However, it has several potential mechanisms of action, which is thought to be the enhancement of GABAergic and a decrease in glutamatergic neurotransmission.[7] To date, the definite mechanism of action of LEV in reducing tremor is not clearly understood. It is suggested that Levetiracetam may possibly act via an influence on the increment of GABAergic activity and also the decline of glutamatergic neurotransmission and excitotoxicity.

Levetiracetam is not only effective in ET but also it is useful for different types of tremor of neurological disorders. The efficacy of LEV in holmes', intention, cortical myoclonic tremor and tremor in multiple sclerosis seems to be promising in some case reports but needs to be investigated in larger patient groups.[8,9]

In a double-blind, placebo controlled trial of Bushara et al., the effect of single dose of 1000 mg LEV on essential tremor was investigated in 24 patients and they showed significant hand tremor reduction for at least 2 hours by using accelerometry and functional tests.[10]

On the contrary, the study of 15 patients diagnosed with ET during the treatment of 500-3000 mg/day during a 5-week slowly titration phase displayed that the analysis of tremor rating scale revealed a statistically insignificant trend for all data.[11]

Further randomized and blinded studies with a larger cohort of patients and basic research must be performed in order to exactly elucidate the antitremor effect of LEV.

Consequently, this case demonstrates that LEV can be alternative option in the treatment of patients diagnosed with ET whom propranolol and primidone had to be discontinued due to unresponsiveness and severe side effects.

REFERENCES

1. Whaley NR, Putzke JD, Baba Y, Wszolek ZK, Uitti RJ. Essential tremor: phenotypic expression in a clinical cohort. Parkinsonism Relat Disord 2007; 13(6):333–9.
2. Louis ED. Clinical practice: Essential tremor. N Engl J Med 2001; 345(12):887-91.
3. Fahn SE, Tolosa E, Marin C. Clinical rating scale for tremor. In: Jankovic J, Tolosa E, eds. Parkinson's Disease and Movement Disorders, 2nd edn. Baltimore: Williams & Wilkins, 1998:225-34.
4. Johannessen Landmark C. Antiepileptic drugs in non-epilepsy disorders: relations between mechanisms of action and clinical efficacy. CNS Drugs 2008; 22(1):27-47.
5. Ondo WG. Essential tremor: treatment options. Curr Treat Options Neurol 2006; 8(3):256-67.
6. Sanz-Cartagena P, Fossas P, Floriach-Robert M, Cano A, Palomeras E. Effectiveness and safety of levetiracetam in patients with essential tremor: data from an open 11-week follow-up trial. Rev Neurol 2007; 45(3):134-6.
7. Kralic JE, Criswell HE, Osterman JL, et al. Genetic essential tremor in gamma-aminobutyric acidA receptor alpha1 subunit knockout mice. J Clin Invest 2005; 115(3):774-9.
8. Saponara R, Greco S, Proto G, Trubia T, Domina E. Levetiracetam improves intention tremor in fragile x-associated tremor/ataxia syndrome. Clin Neuropharmacol 2009; 32(1):53-4.

9. Ferlazzo E, Morgante F, Rizzo V, et al. Successful treatment of Holmes tremor by levetiracetam. Mov Disord 2008; 23(14):2101-3.
10. Bushara KO, Malik T, Exconde RE. The effect of levetiracetam on essential tremor. Neurology 2005; 64(6):1078-80.
11. Elble RJ, Lyons KE, Pahwa R. Levetiracetam is not effective for essential tremor. Clin Neuropharmacol 2007; 30(6):350-6.