Movement Disorders
Vol. 20, No. 5, 2005, pp. 640–644

Letters to the Editors

Levetiracetam for the Treatment of Essential Tremor

We read with interest the recent article by Handforth and Martin,[1] "Pilot Efficacy and Tolerability: A Randomized, Placebo-Controlled Trial of Levetiracetam for Essential Tremor." We also performed a pilot study of levetiracetam (LEV, Keppra) for essential tremor (ET) in 6 ET patients to assess its safety, tolerability, and preliminary efficacy using an open-label design and found similar results. The primary outcome measure for our study was the change in the Fahn–Tolosa–Marin (FTM) rating scale from baseline to endpoint. Secondary outcome measures included the Clinical Global Impression (CGI) scale and Epworth Sleepiness Scale (ESS), the latter performed due to the association of somnolence and LEV.[1,2] A baseline score of 15 on the FTM rating scale was required for study inclusion. LEV was titrated by 250 mg/day every 4 days up to a maximum of 3,000 mg per day. Adjunct medications for tremor were permitted but were maintained at a stable dose for 4 weeks before the screening visit and throughout the study. Patients were evaluated at baseline, and on days 12, 24, 36, and 48. Doses of LEV could be stabilized or reduced at study visits according treatment efficacy and side effects. Last observation carried forward (LOCF) was used for patients who dropped out of the study.

A total of 6 patients enrolled in the study (5 men, 1 woman; average age, 64.7 ± 14.5 years). All patients exhibited upper extremity postural tremor; 1 patient also had a voice tremor, and 1 had head tremor. The mean dose of LEV at endpoint, including LOCF for dropouts, was 1,500 mg ± 1,183 mg. A total of 3 patients withdrew from the study: 2 due to somnolence (days 9 and 12, dose = 500 mg) and 1 due to lack of efficacy (day 24, dose = 1,000 mg). For patients who completed the study, the mean dose of LEV at day 48 was 2,333 mg ± 1,155 mg. The mean baseline and endpoint tremor scores using the FTM scale were 35.5 ± 21.4 and 34.8 ± 22.3, respectively ($P = 1.0$). CGI results revealed that LEV use did not result in a reduction of tremor or improvement in the overall condition. The global impression of change at endpoint was "unchanged" in 2 patients and "minimally worse" in 4 patients, whereas the therapeutic effect was "minimal" in 1 patient and "unchanged or worse" in 5 patients. ESS scores did not change significantly during the study (ESS = 9.0 ± 6.0 at baseline, and 11 ± 8 at endpoint, $P = 1.0$ at all measures), although the study was limited by the small sample size.

While preclinical studies, case reports, and open-label pilot studies suggest that LEV may be useful in treating various movement disorders, including myoclonus,[3] dystonia,[4] and levodopa-induced dyskinesia in Parkinson's disease,[1] our study did not find that LEV had a beneficial effect in reducing ET. Because the double-blind, placebo-controlled study by Handforth and Martin was designed to detect a mean 30% reduction in composite tremor scores, a negative result does not preclude a lower level of efficacy. In our study, no patient considered LEV to be effective in treating tremor or elected to remain on the medication after study conclusion. At endpoint, the global impression of change was unchanged or minimally worse in all patients.

Kelly L. Sullivan, MSPH
Department of Neurology
Parkinson's Disease and Movement Disorders Center
University of South Florida
Tampa, Florida

Robert A. Hauser, MD
Department of Neurology
Department of Pharmacology and Experimental Therapeutics
Parkinson's Disease and Movement Disorders Center
University of South Florida
Tampa, Florida

Theresa A. Zesiewicz, MD*
Department of Neurology
Parkinson's Disease and Movement Disorders Center
University of South Florida
Tampa, Florida
**E-mail: tzesiewi@hsc.usf.edu*

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Published online 8 March 2005 in Wiley InterScience (www.interscience.wiley.com). DOI: 10.1002/mds.20437