

The use of levetiracetam in post-neurosurgical patients with refractory epilepsy

Chen-Nen CHANG, Mei-Yun CHENG, Tony WU

Chang Gung Memorial Hospital, Taipei, Taiwan

Background and Objective: Newer antiepileptic drugs (AEDs) that are devoid of hepatic metabolism (e.g. levetiracetam [LEV], gabapentin) are recommended in neurosurgery patients with brain tumours because they do not show interactions with anticancer agents.¹ Adjunctive LEV has been found to be efficacious and generally well tolerated in Taiwanese adults with refractory partial-onset seizures.² This study aimed to assess the efficacy and safety of LEV in post-neurosurgical Taiwanese patients with refractory epilepsy.

Methods: This was a retrospective study examining records from 23 post-neurosurgical patients with epilepsy (November 2006 to October 2007). Treatment with adjunctive LEV twice daily was individually tailored to patients with treatment-refractory seizures.

Results and Discussion: Of the 23 patients, 18 were male. Mean \pm SD age at study entry was 40.6 ± 14.6 years; age at seizure onset was 29.5 ± 20.3 years; and seizure frequency/month before initiation of LEV was 6.2 ± 17 (length of seizure history: 4.1 ± 3.6 years). Aetiology was: trauma (n=9), brain tumour (n=6), mesial temporal sclerosis (MTS) (n=5), stroke (n=2). Patients had simple partial (n=4), complex partial (n=5) or secondary generalized tonic-clonic seizures (n=18). Patients received 1 (n=4), 2 (n=10), 3 (n=8) or 4 (n=1) concomitant antiepileptic drugs (AEDs), namely valproate (n=14), topiramate (n=13), carbamazepine (n=6), gabapentin (n=6), phenytoin (n=4), benzodiazepine (n=3), oxcarbazepine (n=3) and lamotrigine (n=3). LEV was initiated at 500 mg/day in 13 patients (4 maintained this dose; 9 increased to 1000 mg/day), and 1000 mg/day in 10 patients (9 maintained this dose; 1 increased to 1500 mg/day). Mean \pm SD maintenance dose of adjunctive LEV was 717 ± 253 mg/day; mean treatment duration was 4.9 ± 3.7 months. Numbers of patients experiencing secondary generalized tonic-clonic seizures, complex partial and simple partial seizures fell from 18, 5 and 4, respectively before LEV to 9, 4 and 4, respectively during LEV treatment. Overall seizure frequency/month decreased from 6.2 ± 17 before LEV to 2.1 ± 7.1 during adjunctive LEV treatment (computed over the entire treatment period). 39.1% (9/23) patients were seizure-free and 73.9% (17/23) had $\geq 50\%$ seizure frequency reduction during adjunctive LEV therapy and the result were higher than the figure reported from the previous LEV study (8.5% and 43.5%).² LEV was effective in a range of neurosurgical aetiologies: trauma (5/9 seizure-free, 2/9 $\geq 50\%$ seizure frequency reduction), brain tumour (2/6 seizure free, 1/6 $\geq 50\%$ reduction), MTS (1/5 seizure-free, 3/5 $\geq 50\%$ reduction), stroke (1/2 seizure free, 1/2 $\geq 50\%$ reduction). LEV was also effective in patients with different types of seizures: Simple partial (4/4 $\geq 50\%$ seizure frequency reduction), complex partial (3/4 $\geq 50\%$ reduction), secondary generalized tonic-clonic seizures (14/18 $\geq 50\%$ reduction). The most frequently-reported adverse events were dizziness and sleepiness. Two patients had increased partial seizures (1 discontinued after 5 months); 2 had non-LEV related adverse events (1 hepatic encephalopathy and 1 abnormal liver function tests; both disappeared after stopping valproate).

Conclusion: Adjunctive LEV was effective and well tolerated in post-neurosurgical Taiwanese patients with refractory epilepsy, in a wide range of aetiologies and seizure types. Compared to the previous study done by Tsai *et al*,² patients with confirmed brain lesion responded better to LEV. Adjunctive LEV was associated with high responder ($\geq 50\%$ seizure frequency reduction; 73.9%) and seizure freedom (39.1%) rates during a mean time of 4.9 ± 3.7 months.

References

1. Michelucci R. Optimizing therapy of seizures in neurosurgery. *Neurology* 2006; 67 (12 Suppl 4): S14-8.
2. Tsai JJ, Yen DJ, Hsieh MS, *et al*. Efficacy and safety of levetiracetam (up to 2000 mg/day) in Taiwanese patients with refractory partial seizures: a multicenter, randomized, double-blind, placebo-controlled study. *Epilepsia* 2006; 47: 72-81.