Seizure (2008) **17**, 64—68

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Levetiracetam monotherapy in juvenile myoclonic epilepsy

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Received 16 December 2006; received in revised form 30 May 2007; accepted 10 July 2007

KEYWORDS
Levetiracetam;
Monotherapy;
Juvenile myoclonic epilepsy;
Idiopathic generalized epilepsy

Summary

Purpose: To describe our experience with levetiracetam (LEV) as initial or conversion monotherapy treatment for juvenile myoclonic epilepsy (JME). Valproate, the usual first line agent for JME, has chronic adverse effects, particularly for women of childbearing potential. Since JME requires lifetime treatment, chronic adverse effects of therapy are important consideration.
Methods: We reviewed the medical records of patients with JME treated with LEV in the first 4 years after marketing. We recorded demographic data, results of EEG and imaging studies, antiepileptic drug (AED) history, LEV initial dose and final dose, side effects related to LEV, and therapeutic response to treatment. We classified JME into definite and probable based on clinical and EEG criteria. The minimum duration of follow up was 1 year.
Results: LEV was the first therapy in 12 patients and the initial appropriate agent in 16. Fourteen patients had been treated with another appropriate AED. Eighty percent (24/30) of patients became seizure free with LEV monotherapy and two additional patients showed improved seizure control. Final therapeutic doses of LEV ranged from 12 to 50 mg/(kg day). Complete seizure control using LEV was not predicted by previous AED use. Treatment failure with valproate also did not predict failure of LEV. Patients with definite JME responded best within the study group (11 of 11 seizure free, $p < 0.05$).
Conclusions: This study supports consideration of LEV for first line treatment of JME and suggests the need for a large prospective trial.

Introduction

Valproate is the standard treatment for adolescents with idiopathic generalized epilepsy.[1—5] However,

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1059-1311/$ — see front matter
doi:10.1016/j.seizure.2007.07.001

chronic valproate therapy is associated with potential long-term adverse effects that include weight gain, hair loss, peripheral edema, and hormonal disturbances (e.g. polycystic ovary syndrome). An alternative treatment is desirable. Based on the early favorable experience with several patients with levetiracetam (LEV), we have used LEV as the initial treatment for all patients diagnosed with juvenile myoclonic epilepsy (JME) for the last 5 years. An important reason for this practice is the more favorable side effect profile in comparison with valproate. Although FDA approval and published clinical trials were restricted to add-on therapy for refractory partial seizures, preliminary data supported the use of LEV in patients with idiopathic generalized epilepsy.[6–8] Recently LEV was approved as an adjunctive therapy for JME; however there are limited data on use of LEV as monotherapy in this condition. In this study we formally reviewed our experience with long-term LEV efficacy in patients with JME.

Methods

Patients

This study initially targeted patient with JME. It included a retrospective medical record review of 43 consecutive patients with JME or probable/potential JME seen by faculty of the Department of Child Neurology at The Monroe Carrol Jr. Children's Hospital at Vanderbilt University Medical Center (VUMC) between January 2001 and August 31, 2004. Search words of *JME*, *juvenile myoclonic epilepsy*, and *levetiracetam* or *Keppra* searched an electronic record file to identify appropriate patients. The inclusion criteria for the purpose of this study included age of onset between 5 and 21 years, treatment with LEV, and diagnosis of definite or probable JME. The classification of JME was not always straightforward. Among patient eventually diagnosed with JME, a clear history of myoclonic jerks was often not obtained by history, even after providing detailed descriptions of the movements and witnessing myoclonic jerks during the examination. Sometimes, the history of myoclonic jerks is only established prospectively when the family bears closer attention. A further difficulty in restricting the study population is the late appearance of myoclonic jerks in patients diagnosed with juvenile absence epilepsy. We therefore examined response to LEV in a larger group of patients with juvenile onset idiopathic generalized epilepsy. The following criteria classified patients as definite or probable JME. Patients classified as *definite JME* had: (1) generalized epilepsy with myoclonic jerks mainly upon awakening or sleep deprivation, with or without generalized tonic–clonic seizures (GTC) and with or without generalized absence seizures; (2) normal intelligence; (3) normal documented neurological examinations; (4) generalized 3–6 Hz spike-wave and/or polyspike-wave discharges on EEG; (5) normal brain imaging (CT or MRI, if performed). *Probable JME* was defined as having the above characteristics except for one of the following: (1) subnormal intelligence, (2) focal EEG findings,[9,10] (3) no clear report of myoclonic jerks, or (4) normal EEG or no EEG on record. It is possible that this group includes patients with juvenile absence epilepsy or epilepsy with generalized tonic–clonic seizures only. We excluded patients with more than one exception and those not treated with LEV. Our final study population consisted of 30 patients with definite or probable JME, who were treated with LEV. Among the 13 patients excluded from the study, two classified as probable JME, were lost in follow up after starting on LEV; four patients with suspected JME were less than 5 years of age; and two patients had never used LEV but appeared in the search because it was a consideration. Five patients that turned up in the search because of the word myoclonus did not have JME, but had other diagnoses which included infantile spasms, benign rolandic epilepsy, sleep myoclonus, symptomatic epilepsy with severe hypoxia at birth, and Angelman syndrome.

Data recording and analysis

The medical record review included a screen for the inclusion criteria, the current age, all AED use (including inappropriate and appropriate AEDs) and specifically valproic acid (VPA) use, AED efficacy, and AED adverse effects. We documented date of initial LEV treatment, initial and final LEV dosages, with a calculation of mg/(kg day) dosing when weight was available, seizure control before and after LEV and duration of LEV use. We considered patients seizure free if they had had no seizures for at least 3 months. Patients were considered improved if they had at least 50% reduction in seizure frequency. We evaluated the relationship between seizure freedom and prior exposure and response to other AEDs and to clinical features of epilepsy. Fisher's exact test was used for group comparison.

Results

Patients and seizure types

Thirty patients met criteria for JME. Ten were male and 20 female. The average age of onset was slightly