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Levetiracetam in the treatment of primary generalised seizures

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Introduction

Levetiracetam (LEV) is a new antiepileptic drug (AED) which has proven to be effective for treating partial-onset seizures [1] and is approved in the USA and Europe as add-on therapy for the treatment of refractory partial seizures [2]. There is currently no information on the long-term efficacy of LEV for treating generalised epilepsy, but there is evidence that it is effective in juvenile myoclonic epilepsy (JME) [3] and in photosensitive epilepsy [4]. In 55 patients with myoclonic, tonic and absence seizures who had failed on other AEDs (in order of frequency: valproate (VPA), carbamazepine (CBZ), phenytoin (PHT), and lamotrigine (LTG)), 12 weeks of LEV treatment resulted in 40% of patients with 100% seizure-freedom and 76% with a reduction in seizures of ≥50% [5]. In a recent study, when 25 patients with refractory generalised epilepsy (13 with JME) were treated with LEV as add-on therapy, 16% of patients became seizure-free [6].

Objective

The aim of this ongoing study is to determine the efficacy of LEV as monotherapy in patients with generalised epilepsy.

Methods

This study is designed to evaluate the efficacy of LEV as monotherapy in patients with generalised epilepsy already taking other AEDs for seizure control.

The study is ongoing with a follow-up to period of 1–2 years.

Patients

Patients with generalised epilepsy who were taking ≥1 AED for seizure control were included (n=13).

Dosing

All patients initially received LEV as add-on therapy, at doses ranging from 1500 mg to 4000 mg daily.

Patients are gradually being switched to LEV monotherapy; concomitant AEDs are being withdrawn.

Results

Patients

Patient demographics, seizure types and AED therapy are shown in Table 1. At study entry, all patients were still experiencing monthly seizures of various frequency despite AED therapy with VPA, LTG or PB. The mean time taken to switch to LEV monotherapy was 3 months. MRI was normal in all 13 patients.

Efficacy

All 13 patients improved both clinically and electroencephalographically after commencing LEV therapy with a ≥50% reduction in seizure frequency (Fig. 1). To date, 4 patients (2 with JME, 1 with absence epilepsy, 1 with tonic-clonic seizures) have received monotherapy for 12 months. All 4 patients on LEV monotherapy are 100% seizure-free; 2 have been seizure-free for 6 months and 2 for 10 months. Of 9 patients still receiving LEV add-on therapy, 6 have been 100% seizure-free for 6–12 months and the remaining 3 have had a reduction in seizures of 50%–75% for 5–6 months.

Tolerability

Three patients receiving LEV as add-on therapy reported mild adverse events (AEs) of somnolence and sedation.

Two young women who had AEs of amenorrhea, weight gain and alopecia whilst receiving VPA before the study, showed a marked improvement in AEs after switching to LEV monotherapy: alopecia and amenorrhoea disappeared and weight gain was reduced.

Table 1 Patient characteristics (n=13)

Patients	
Gender, n	
Male	8
Female	5
Age (years)	
Mean	30
Range	16–32
Seizure types, n	
Absence epilepsy	3
JME	5
Primary generalised tonic-clonic seizures	5
Concomitant AEDs, n	
VPA	7
VPA + LTG	4
PB	1
PB + VPA	1

VPA, valproate; *LTG*, lamotrigine; *PB*, phenobarbital

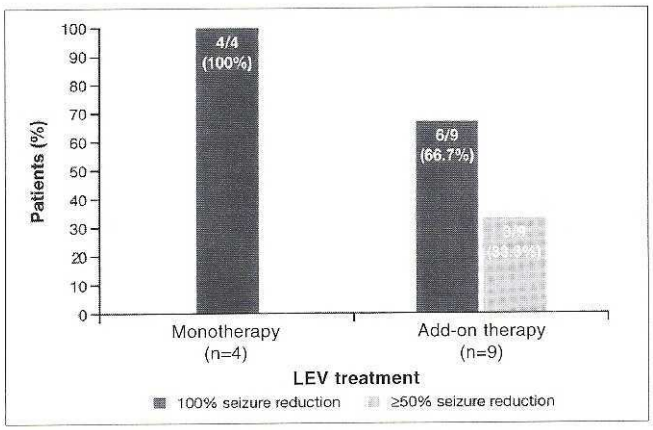

Fig. 1 Seizure reduction in patients treated with LEV monotherapy or LEV add-on therapy

Conclusions

The present study supports previous reports on the efficacy of LEV in the treatment of generalised epilepsy.

Generalised seizures can be treated successfully with LEV used initially as add-on therapy and then as monotherapy after withdrawal of concomitant AEDs.

Withdrawal to LEV monotherapy was well tolerated and was associated with no increase in AEs in this study.

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