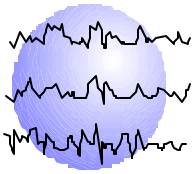
LEVETIRACETAM MONOTHERAPY

Beth Korby, RN C
Patricia E. Penovich, MD
John R. Gates, MD
Deanna L. Dickens, MD
Gerald L. Moriarty, MD



This paper has been prepared specifically for:

American Epilepsy Society Annual Meeting
Boston, MA
December 5 - 10, 2003
Please consider this information to be preliminary findings.

Minnesota Epilepsy Group, P.A.®
225 Smith Avenue N., Suite 201
St. Paul, MN 55102-2534
Phone: (651) 241-5290
Fax: (651) 241-5248

REVISED ABSTRACT

RATIONALE

Leviteracetam (LEV) has been approved for adjunctive use in refractory partial epilepsy. Its pharmacokinetic advantages and unique mechanism of action have led to increased use. Sporadic reports of LEV efficacy in monotherapy led us to review what our experience has been over the last 3 years in a large population of patients with refractory epilepsy, new onset epilepsy and epilepsy secondary to newly diagnosed CNS neoplasm.

METHODS

A retrospective chart review of patients receiving LEV was performed for monotherapy patients. Data was tabulated for age, gender, IQ, behavioral problems (BP) and psychological history, medication history, seizure frequency, adverse effects (AE), LEV doses and serum levels.

RESULTS

50 patients reached LEV monotherapy (LEV-M): 3 (6%) de novo, 47 (94%) transitioned from another AED. 9 (18%) had primary CNS neoplasms. 43 (86%) remain on LEV-M, 2 (4%) required additional AEDs. 5 (10%) discontinued LEV due to AEs, BPs, or poor control (Figure 1). Doses ranged from 250 to 3000 mg per day (mean 1,462.4, median 1,500). Serum levels ranged from 2-37 ug/ml (mean 16.4, median 15.5). Seizure freedom is present in 38 (76%) over 2-40 months (mean 20.7, median 20). Seven tumor patients (78%) are seizure free. AEs were reported by 26 patients (52%) at sometime, resolving with lowering dose in 6 (23%). Only 2 (7%) discontinued LEV due to AEs. Reported AEs were sedation/lethargy 13 (26%), dizzy/lightheaded 6 (12%), hand tremor 4 (8%), headache 3 (6%), ataxia 2 (4%), and single reports of decreased appetite, insomnia, being tense, decreased memory, decreased cognition, acne, drunk feeling, clumsy, altered depth perception, weight gain, decreased libido, itching, hair thinning, and increased dreaming. BPs were present in 18 (36%) prior to LEV-M. Of these, 10 (56%) had no change in BPs, 6 (33%) had improved behavior and 2 (11%) had increased behaviors. Of the 6 who improved, the BP diagnosis was depression or mood disorder in 5. 32 (64%) had no prior BPs and 4 (12%) of these developed BPs on LEV-M and LEV was discontinued in 1.

CONCLUSION

LEV-M offers significant benefit for patients with epilepsy. Seizure control can be excellent. Most AEs are temporary and well tolerated. Those with a previous history of behavioral or psychiatric problems did not experience intolerance to LEV at any increased rate. A subgroup with depression and mood swings improved. LEV-M may be achieved without difficulty in patients with refractory epilepsy and in patients with primary CNS neoplasms.

Epilepsia 44 Suppl. 9:108 (Abst. 1.306), 2003

INTRODUCTION

Keppra has been an effective add-on AED well tolerated by most patients. We have been using Keppra in monotherapy for some time. There have been no controlled trials and few reports of its efficacy in monotherapy. We reviewed our experience at Minnesota Epilepsy Group, P.A. of LEV-M over a 40 month period of time after LEV approval.

METHODS

We reviewed the charts of 50 active adult patients who are or were on LEV-M for efficacy, AEs and behavioral problems (BP). We looked at dosages and levels to see if they had any correlation with outcomes. 9 of the 50 patients had primary CNS neoplasms. Their information was reviewed as a subgroup as well.

IQ testing was not available on all patients. They ranged from profoundly retarded to highly functioning college educated adults.

Patients were screened for the following BPs: irritability, aggression, change in mood, and psychosis.

RESULTS

- Patient age at time of chart review was 17-67 years (mean 38.2).
- 27 of the patients were female, 23 were male.
- Prior to LEV-M, 18 were seizure free but were changed to LEV due to prior AED AEs. 32 were switched due to poor seizure control.
- On LEV-M, 38 (76%) became seizure free and 12 (24%) continued to have seizures. Of these 12, 1 was noncompliant, 3 had seizures evolving from complex to simple partial seizures, 2 required addition of another AED, 1 discontinued LEV, and 5 continued with infrequent seizures. (Figure 2)
- 9 patients had primary CNS neoplasms. 7 (78%) of these remain seizure free, 6 (67%) reported AEs, 2 resolved; 3 (33%) developed BPs, 1 resolved; 1 with mood/depression problems was felt more associated with diagnosis than LEV. (Figure 3)
- There were no serious AEs leading to hospitalization or death. 23% of AEs resolved on lower dose. 23% resolved without dose change over time. Only 2 (7%) discontinued LEV due to AE. AEs included: sedation n=13 (26%), dizzy/lightheaded n=6 (12%), hand tremor n=4 (8%), headache n=3 (6%), ataxia n=2 (4%) and single reports of decreased appetite, insomnia, being tense, decreased memory, decreased cognition, acne, drunk feeling, clumsy, altered depth perception, weight gain, decreased libido, itching, hair thinning, and increased dreaming. (Figure 4)
- BPs were present in 18 (36%) prior to LEV-M. Of these, 10 (56%) had no change in BPs, 6 (33%) had improved behavior and 2 (11%) had increased behaviors. Of the 6 who improved, the BP diagnosis was depression or mood disorder in 5.

- 32 (64%) had no prior BPs. Of these, 4 (12%) developed BPs on LEV-M. 1 resolved over time, 1 with depression was thought more associated with brain tumor diagnosis than LEV, 1 discontinued LEV due to BPs and 1 was lost to follow up. (Figure 5)
- There were no psychoses.
- There was no clear correlation for BPs in relation to dose or serum levels. (Figure 6)
- There was no clear correlation of seizure freedom with dose or serum levels. (Figure 7)

CONCLUSIONS

- LEV-M offers significant benefits for patients with epilepsy.
- Seizure control was excellent in 76%.
- Most AEs are temporary and were tolerated.
- Those patients with a previous history of behavioral or psychiatric problems did not experience an increase in the rate of intolerance to LEV compared to those with no prior BPS.
- There is no clear correlation of dose or serum level with seizure control or development of BPs.
- A subgroup with depression and mood swings improved.
- Those with primary neoplasms had no significant difference in seizure control or intolerance to LEV compared to patients without tumors or the whole group.
- LEV-M may be achieved without difficulty in patients with refractory epilepsy and in patients with primary CNS neoplasms.

Keppra Treatment History

Figure 1

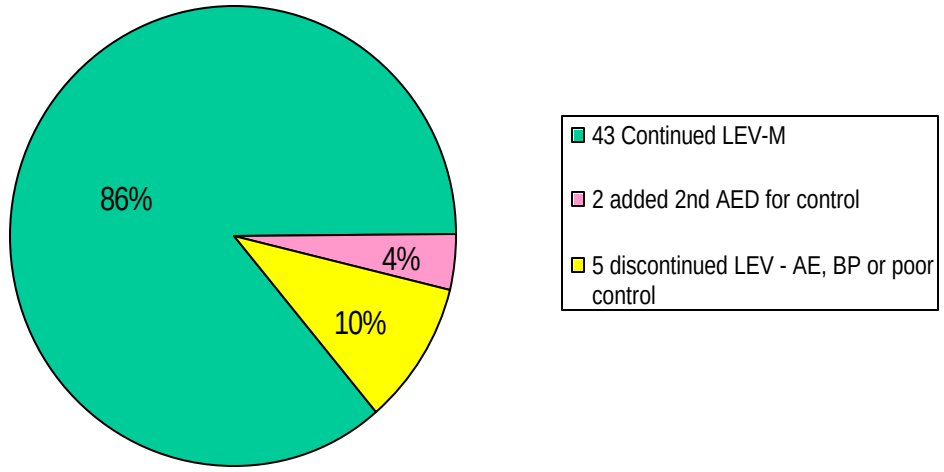
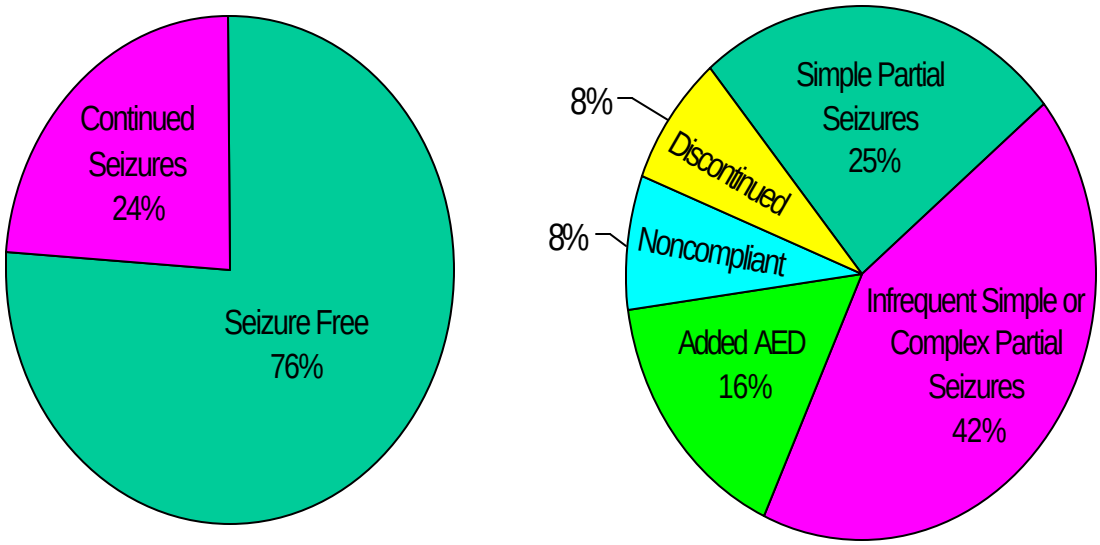


Figure 2

Seizure Clinical Course



A: All Patients

B: 12 (24%) Patients who continue to have seizures

Figure 3 **Clinical Course in Patients with Primary CNS Neoplasms**

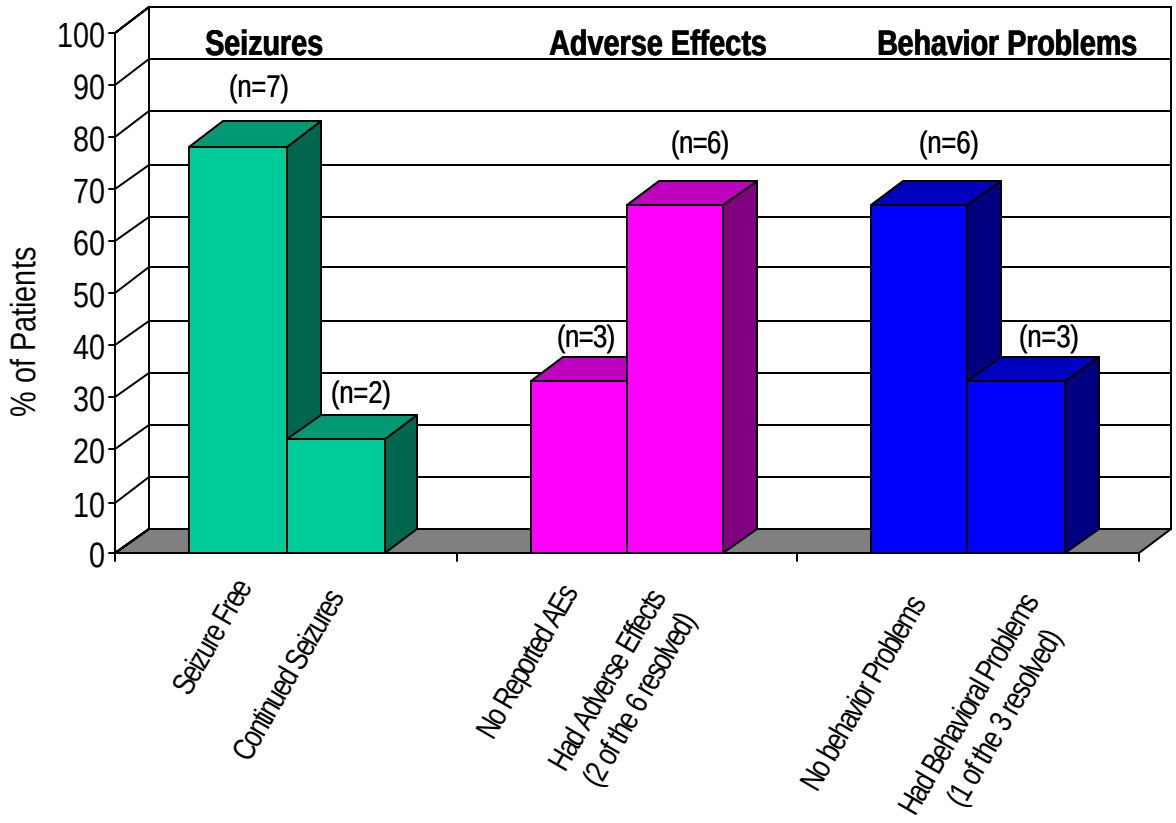


Figure 4 **Reported Adverse Effects of LEV-M**

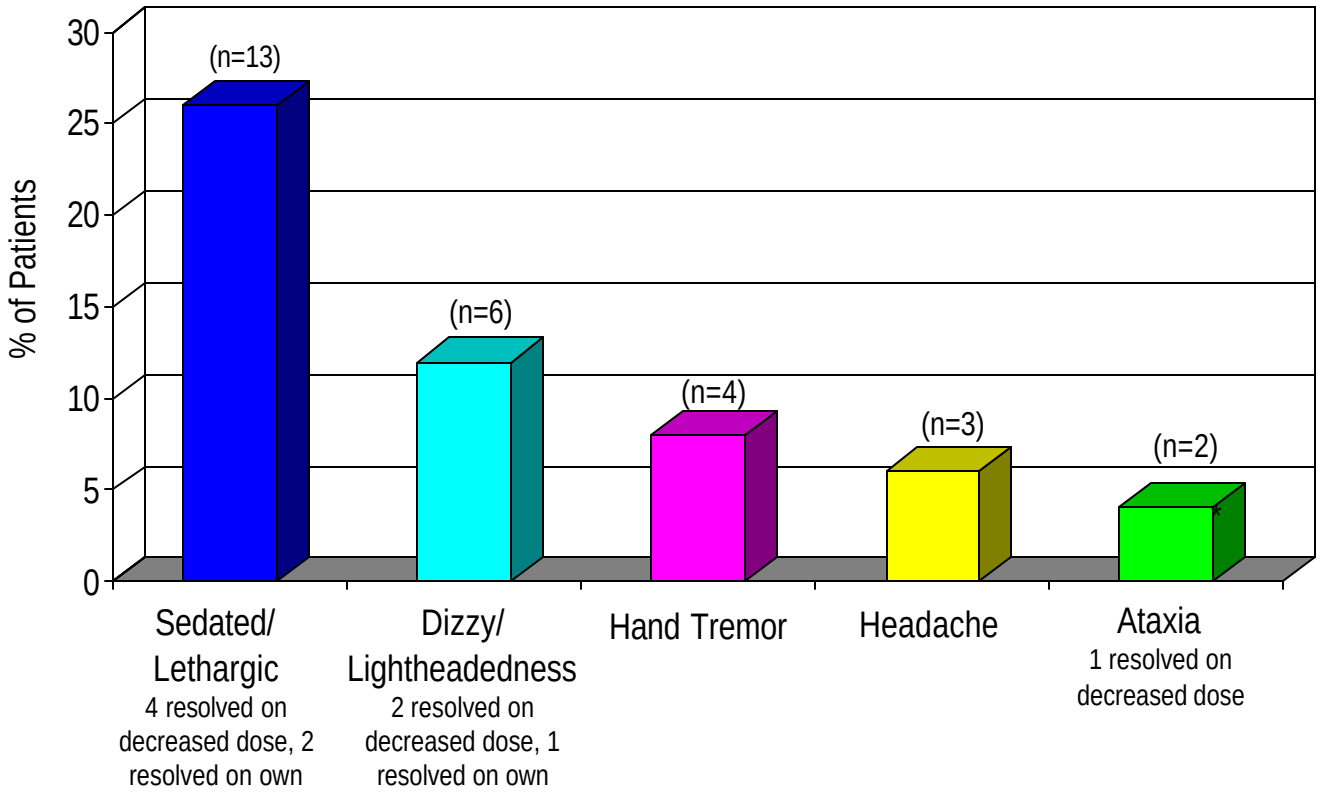


Figure 5

Behavior Problems (BP): Clinical Course In All Patients

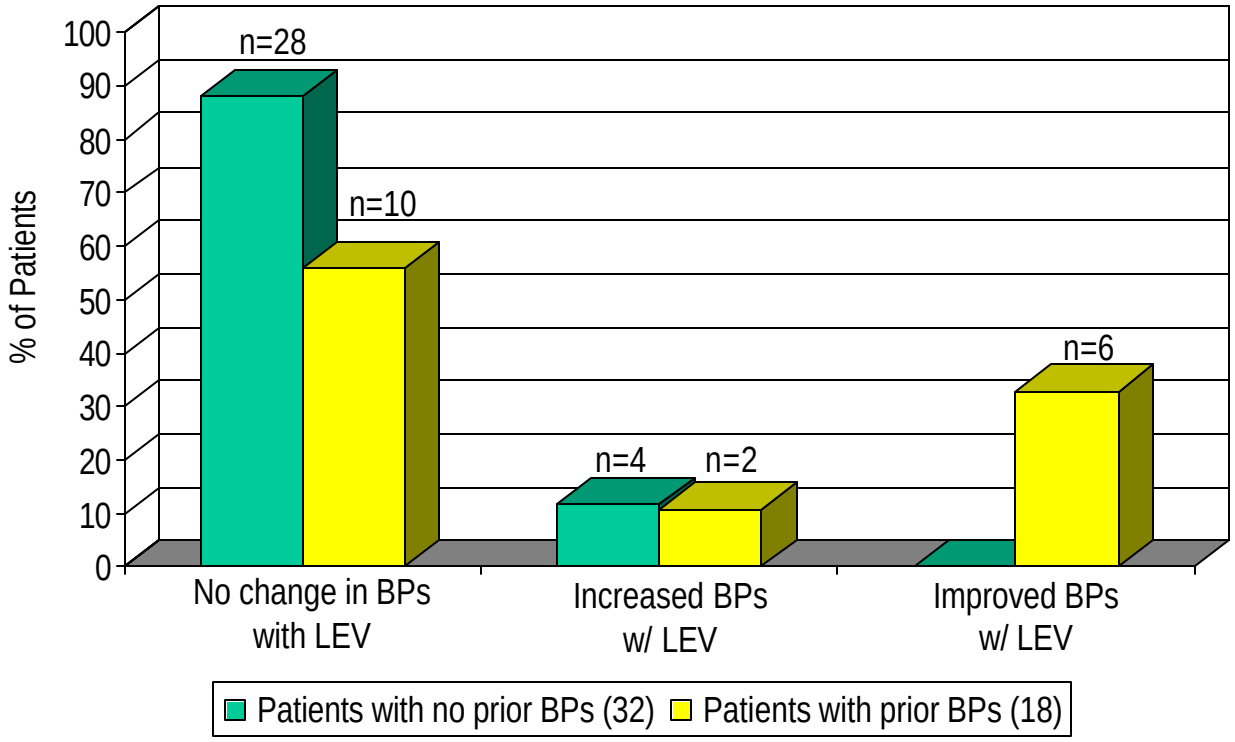


Figure 6

Behavioral Problems (BP): Serum Levels and Dosage

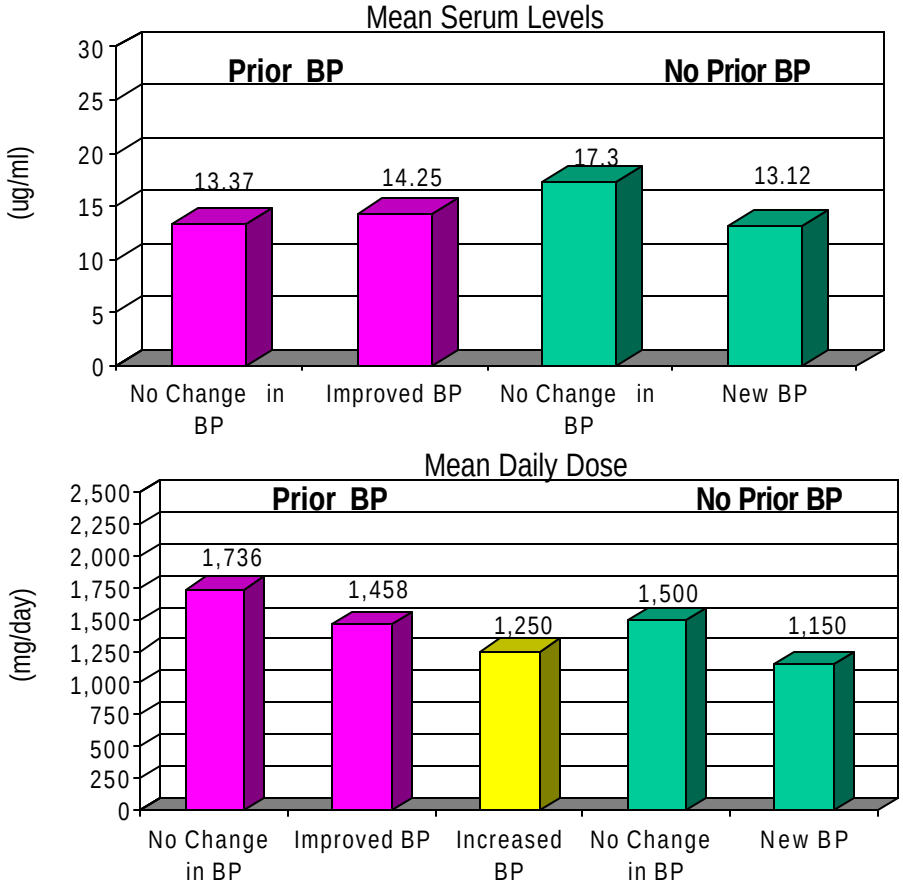


Figure 7

Seizure Control: Serum Levels and Dosage