CLINICAL EXPERIENCE WITH LEVETIRACETAM TREATING REFRACTORY, SYMPTOMATIC SEIZURES IN CHILDREN

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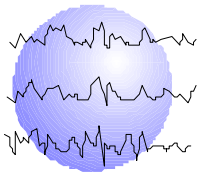

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ABSTRACT

RATIONALE: Levetiracetam (LEV) has a unique preclinical profile separating it from other antiepileptic medications (AEM). LEV may benefit children who have failed to respond to previous AEM treatment. However, little is known about the use of LEV in children < 12 years of age. We have reviewed our records and report our experience on dose, efficacy and adverse side-effects of LEV in children.

METHODS: Charts were randomly selected until 50 children meeting the following criteria were found: 1) age < 12 y.o.; 2) refractory epilepsy; and 3) at least six months follow-up after initial treatment with LEV. Charts were then reviewed for demographics, seizure types/frequency, epilepsy syndrome, dose and titration rate of LEV, efficacy, adverse effects (AE), previous/current AEMs and etiology of seizures.

RESULTS: 30 girls, 20 boys, age 1-11 y.o. (median 6) were treated with LEV, initial dose 3.7-22 mg/kg/day (median 9). The maximum dose was 7.3-100 mg/kg/day (median 51, mean 46). All had symptomatic epilepsy, failed to respond to 1-15 previous AEM (median 8, mean 7), and most had partial onset seizures. Children with Lennox-Gastaut (3), Landau-Kleffner (3), Epilepsia Partialis Continua (1), and infantile spasms (1), were included. Efficacy: 8 were seizure free, median dose 44 mg/kg/day, had failed a median of 5 previous AEM. 4 of these children have been transitioned to LEV monotherapy. An additional 6 children had > 50% decrease in seizure frequency, 4 of these have > 75% decrease in seizures. Nineteen children have continued LEV treatment with < 50% improvement in seizure control, but other benefits. Improvements were seen in partial onset seizures, atypical absence, tonic, tonic-clonic, and myoclonic seizures. Eighteen children have discontinued LEV, 8 for lack of efficacy (median dose 56 mg/kg/day), and 10 for AE. Of 10 discontinuations for AE, 9 were for adverse behavior (median dose 50 mg/kg/day). Six of 9 had a positive history of behavior problems and one was seizure free. One child discontinued due to rash. There were no systemic AE.

CONCLUSION: LEV demonstrated efficacy and tolerability in children with refractory epilepsy. All seizure types responded. Almost one of every 6 refractory patients became seizure free.

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INTRODUCTION

Levetiracetam (LEV), a novel anti-epileptic medication (AEM), was first introduced to the world with its launch in the United States in April 2000. It was FDA approved for adjunctive treatment of partial onset seizures in adults. The pivotal studies showed LEV to be effective and well tolerated. At the time of its approval, only one small clinical trial involving children was in progress. At the Minnesota Epilepsy Group, LEV has been prescribed to pediatric patients of all ages and seizure types due to intractability and/or adverse effect profile with other AEMs. To date, little information regarding the use of LEV in 115 young children has been published. We describe our clinical experience with LEV in children under the age of 12 years.

METHODS

Medical records for all children meeting 2 inclusion criteria: 1) less than 12 years old, 2) at least 6 months follow-up from an initial dose of LEV, were reviewed for demographics, baseline seizure type(s) and frequency, cognitive function, seizure etiology, past and current behaviors, and previous epilepsy treatments. Dose and titration of LEV, tolerability, and efficacy of LEV were evaluated on an intent to treat basis.

RESULTS

Records on 122 children meeting inclusion criteria were reviewed. Seven children were excluded, lost to follow-up or insufficient data. Results are reported for the remaining 115 children.

CONCLUSIONS

- In children <12 y.o. with difficult to treat epilepsy (median 7 previous AEM failures)
    - 1 out of 6, seizure free (16%)
    - 8/18 = 44%, seizure free reduced to monotherapy
    - 44/115 = 38%, ³ 50% reduction in seizures
    - 25/115 = 22%, continued LEV with some benefit

- Most Common Adverse Effect
    - Worsening of behavior/mood 31%
      - 92% had history of behavior/mood disturbance
    - However, 29/65 (44%) children with a history of behavior/mood disturbance did not have a worsening when treated with Levetiracetam

- No Systemic Adverse Side Effects were seen

DEMOGRAPHICS

N=115

Age: Median = 5.5 y.o. (Range: 1-11 y.o.)

Sex: 61 girls, 54 boys

History of Mood/Behavior Disorders: 65/115 (55%)

Cognitive Impairment/Developmental Delay: 100/115 (87%)

Seizures: Partial onset 84 (73%); Generalized 31 (27%)

Previous AEM: Median 7 (Range: 0-15)

Epilepsy Syndromes:

Lennox-Gastaut Syndrome (LGS)	**n=12**
Landau-Kleffner Syndrome (LKS)	**n=2**
Epilepsia Partialis Continua	**n=1**

EFFICACY

Percent - Seizure Reduction

	< 50%	**50-99%**	**100%**
Partial n=84	**55 (65%)**	**14 (17%)**	**15 (18%)**
Generalized n=31	**16 (51%)**	**12 (39%)**	**3 (10%)**
LGS n=12	**5 (42%)**	**5 (42%)**	**2 (16%)**
LKS n=2	**0 (0%)**	**1 (50%)**	**1 (50%)**
ALL	**71 (61%)**	**26 (23%)**	**18 (16%)**

ADVERSE SIDE EFFECTS

- **36/115 (31%) Worsening Behavior/Mood**
    - **19/36 - Discontinued due to adverse behavior/mood**
    - **33/36 - History of "Bad Behavior"**
    - **18/36 - Previously discontinued AEMs for "Bad Behavior"**
- **8/115 (6%) Sleepy/Fatigue (2 d/c LEV)**

REASON FOR DISCONTINUATION

N=47

- **20 (42%) Ineffective**
- **19 (40%) Worsening Behavior**
- **2 - Fatigue**
- **1 each - Rash, ↓ Appetite, Decline in Memory, "Body Bouncing"**