Evaluation of Efficacy and Tolerability of Lacosamide in Children with Drug-Resistant Epilepsy: A Multicenter Cohort Study

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INTRODUCTION

- Lacosamide (LCM) is an antiseizure agent that targets voltage-dependent sodium channels. It has a predictable pharmacokinetic profile with a high oral bioavailability and a low potential for clinically relevant pharmacokinetic drug-drug interactions.
- LCM is indicated for the treatment of focal (partial-onset) seizures in patients ≥4 years of age in the United States and the European Union.
- The most common side effects include dizziness, vertigo, double vision, nausea, and headaches.
- Pediatric approval of LCM is based on extrapolation of efficacy data from adolescents and adults and safety and pharmacokinetic data from open-label studies of adjunctive LCM therapy in children. There is less data from randomized controlled trials to guide the treatment of epilepsy in pediatric patients than in adults.

OBJECTIVES

- There are very few studies in the literature on the efficacy and tolerability of lacosamide, which is used in the treatment of patients with drug-resistant epilepsy in the world and in our country.
- In this study, we aimed to contribute to the literature by retrospectively examining the efficacy and tolerability of lacosamide in patients with drug-resistant epilepsy.

MATERIALS & METHODS

- After the approval of the ethics committee, 289 patients aged 1 month to 18 years, followed by the Pediatric Neurology Outpatient Clinic from 14 centers between January 2014 and June 2021, were included in the study.
- Demographic data of patients, epilepsy type, epileptic syndrome diagnoses, additional diagnoses, MRI findings, seizure frequency, EEG findings, clinical and EEG responses after treatment initiation, LCM initial and maintenance doses, other anti-seizure drugs used, concurrent use of sodium channel blocker anti-seizure drugs, and observed side effects (one or more) were recorded.
- Patients 1 month to 18 years of age with confirmed epilepsy with focal or generalized seizures that could not be controlled despite treatment with two or more concurrent or sequential anti-seizure medications were included in the study.
- At the initiation of LCM treatment, he must have had two or more seizures in the previous 4 weeks and must have taken a stable dose of one to three anti-seizure medications for at least 1 week. The use of a vagus nerve stimulator was allowed and did not count as anti-seizure medication. Patients who underwent a ketogenic diet and epilepsy surgery were included.
- **Analysis of Data:** SPSS 26.0 was used for statistical analysis. Descriptive statistics of evaluation results; numbers and percentages were given for categorical variables, mean, standard deviation, minimum and maximum were given for numerical variables. The conformity of the data to the normal distribution was determined by Kolmogorov-Smirnov and Shapiro-Wilk. Pearson Chi-square or Fisher's Exact Test was used to compare categorical variables, and Mann-Whitney U test was used to compare numerical variables. McNemar-Bowker Test was used to determine the difference between seizure frequency before medication and seizure frequency after medication. In all statistical analyses, the significance value was taken as $p<0.05$.

RESULTS

- The mean age of the patients included in the study was 13.52 ± 0.51 (1-24), 52.9 % (n = 153) of the patients were male (Table 1). The mean age of onset of LCM was 10.41 years ± 4.73 (1-18). The mean starting dose was 2.63 mg/kg/g, while the mean daily effective dose was 6.87 mg/kg/day (2.3-12) throughout the treatment period. The oral tablet form of LCM was found to be 88.9% (n=257) easy to use and tolerate. A significant decrease in seizure frequency was found at the 3rd month of additional LCM treatment [($p<0.001$), Table 2]. The rate of treatment-emergent adverse events (TEAE) was 23.9% (n = 69), the most common somnolence was 10.4%(n=30, Table 3). While no change was detected in 62.6%(n:181) electroencephalographically, there was more than 50% improvement in 3.5% (n:10) and complete recovery in 3.8% (n:11). Treatment was continued in 67.8% (n=196) of the cases, and treatment was discontinued in 19.7% (n=57) because there was no change in seizure frequency.

CONCLUSIONS

- The results of our study: although they are similar to the results in the literature, they contain the highest number of cases in studies conducted on children. provides preliminary evidence for the efficacy of LCM in children with refractory epilepsy. Randomized, controlled trials are needed to confirm efficacy and fully investigate side effects in children with refractory epilepsy.
- **Our findings support the hypothesis that adjuvant LCM is effective, safe, and tolerable at doses up to 12 mg/kg/day in children with resistant epilepsy.**

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