4 Efficacy of Lacosamide in Children and Adolescents with Drug-Resistant Epilepsy and Refractory Status Epilepticus: A Systematic Review

Adapted from Ortiz de la Rosa JS, Ladino LD, Rodríguez PJ et al. *Seizure*. 2018 Mar;56:34-40.

Lacosamide is approved for focal drug-resistant epilepsy as an add-on treatment in adult patients. Due to the growing evidence of its use, safety and efficacy in children, the efficacy and tolerability of Lacosamide in focal and generalized drug-resistant epilepsy and refractory status epilepticus in the pediatric population was assessed.

A thorough systematic review from January 2008 to January 2017 was done. The efficacy of Lacosamide in children with drug-resistant epilepsy and refractory status epilepticus was the primary outcome. The efficacy and adverse events due to Lacosamide were extracted and systematically reported.

A meta-analyses was not done due to limited available data. Twenty-six articles met the eligibility criteria and described outcomes in 797 patients (57% male). The studies were mainly retrospective (69%) and small series (84%).

Result showed that:

- 51% of patients had ≥50% seizure reduction on average
- 24% was the mean seizure freedom rate
- Dizziness, sedation, gastrointestinal upset, mood and behavioral changes were the main side effects
- Half of the patients with Lennox Gastaut syndrome showed ≥50% seizure reduction

Based on the efficacy on seizure control and safety profile, Lacosamide as an add-on therapy proved to be a good option in pediatric patients with focal drug-resistant epilepsy and refractory status epilepticus.

Adjunctive Lacosamide is a good option in focal drug-resistant epilepsy pediatric patients, given its efficacy on seizure control and safety profile

6566136

LACOSAM

Epilepsy Episodes

Issue 4 - Focus on Focal Onset Seizures in Children

CONTENT

1 Efficacy and Tolerability of Oral Lacosamide as Adjunctive Therapy in Pediatric Patients with Pharmacoresistant Focal Epilepsy

Adapted from Gavatha M, Ioannou I, Papavasiliou AS. *Epilepsy Behav.* 2011 Apr;20(4):691-3.

Adjunctive Lacosamide treatment results have been reported in 18 pediatric patients with pharmocoresistant focal epilepsy.

All the patients were receiving one to three other antiepileptic drugs concomitantly and all presented with severe forms of focal epilepsy with or without secondary generalization.

The final dose of Lacosamide after slow titration ranged between 1.7 and 10 mg/kg when administered orally. The mean duration of treatment was eight months (ranging from 3 weeks to 17 months).

Assessment of effectiveness of the treatment was done at two points within the one year interval. Effects of LCM were assessed at two different times, at an initial short-term assessment and at a long-term evaluation 1 year after the first assessment. The first assessment ranged from 3 to 8 months (mean = 5 months). One year after the first evaluation, the records and seizure diaries of the same group of patients were reviewed.

Greater than 50% reduction in seizure frequency was reported in 36% patients in the initial short-term and in 20% following long-term assessment.

In both evaluations, the side effects of mainly somnolence and irritability were seen in 39% of the patients. Lacosamide treatment is safe with the doses up to 10 mg/kg/day in children, without any major side effects as per the data ascertained.

Adjunctive Lacosamide therapy is safe up to 10 mg/kg/day dosage in pediatric patients with pharmacoresistant focal epilepsy

2 Efficacy and Tolerability of Lacosamide as an Adjunctive Therapy in Children with Refractory Partial Epilepsy

Adapted from Pasha I, Kamate M, Didagi SK. *Pediatr Neurol.* 2014 Oct;51(4):509-14.

The efficacy of adjunctive Lacosamide therapy was examined in children with refractory partial epilepsy in this unicentre prospective study.

A thirty months study was done between November 2011 and May 2014, at a tertiary care hospital. A total of seventy-nine children with refractory partial epilepsy (age ranging from 5 to 15 years) who have failed therapy with two or more antiepileptic drugs, and were using Lacosamide as adjunctive therapy were chosen for the study. An oral dose of 25 mg of Lacosamide was given for one week followed by 50 mg, given two times a day for the rest of the period.

Assessment of the effectiveness and tolerability was made at every visit of titration, for a maintenance period of 3 months, and two follow-up visits were done at monthly intervals.

Tests like the liver function test and electrocardiogram were done in the children before the Lacosamide treatment and at the end of third month of the therapy. Adverse events were recorded in a predesigned proforma as observed by the patient caregivers or the investigator.

Seventy-nine patients having uncontrolled partial epilepsy that met the inclusion and exclusion criteria were selected from 531 epileptic children. 53 out of 79 (67.0%) children were boys.

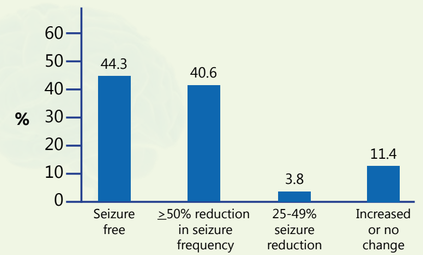
The mean age of the patients was 8.8 ± 3.1 years, ranging from 5 to 15 years while the mean age at the onset of seizure was 6.4 ± 3.5 years. 24.2 ± 9.8 kg was the mean weight of the patients.

The mean dose of Lacosamide given was 4.1 mg/kg. Three of the patients (3.8%) were seen with adverse effects such as vomiting, aggressive behavior and poor response respectively and they were excluded from the study.

Among those seventy-six patients that entered the maintenance period, 35 patients (44.3%) were seizure free, 32 patients (40.6%) showed ≥50% reduction in seizure frequency, 3 patients (3.8%) showed 25-49% seizure reduction, and 9 patients (11.4%) were seen with either increased seizure frequency or had no change at all.

In children with refractory partial epilepsy, Lacosamide is an effective add-on antiepileptic drug and is well tolerated.

Figure 1. Seizure reduction in the maintenance period



Adjunctive Lacosamide therapy is efficacious and well tolerated in children with refractory partial epilepsy

3 Lacosamide in Pediatric and Adult Patients: Comparison of Efficacy and Safety

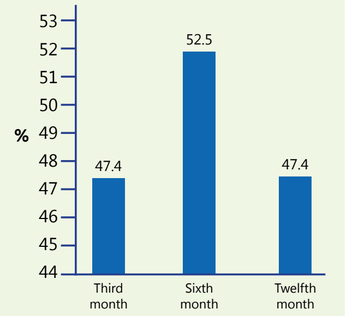
Adapted from Verrotti A, Loiacono G, Pizzolorusso A et al. *Seizure.* 2013 Apr;22(3):210-6.

The safety and effectiveness of adjunctive Lacosamide therapy was surveyed in pediatric and adult patients with uncontrolled epilepsy in a multicenter prospective study but we will focus on the pediatric findings in this study.

This study was performed at 16 Italian and 1 German neurologic center from September 2010 to December 2011. In patients less than 16 years of age, Lacosamide was added at a starting dose of 1 mg/kg/day to the baseline therapy which was then titrated to the target dose that ranged from 3 to 12 mg/kg/day.

The patients then entered into a 12-month of maintenance period after the completion of the titration period. Follow-ups were done at 3, 6 and 12 months.

Figure 2. Month wise 50% reduction in seizures



Based on the changes in the seizure frequency at 28 days from baseline, the primary assessment of efficacy was estimated at 3, 6 and 12 months and as follows: number and proportion of 100% responders, 50% responders, non-responders and worsening patients. Safety assessment was done at 3, 6 and 12 months.

Fifty-nine pediatric patients with uncontrolled generalized and focal epilepsy fulfilled the inclusion criteria. At the three month assessment, a 50% reduction in seizure frequency was seen in 47.4% of the pediatric patients. The 50% responders observed at the sixth and twelfth month of follow up were 52.5% and 47.4% respectively.

Adverse effects were seen in 30.5% patients during the treatment period in which dyspepsia was the most common. Management with Lacosamide can be safe and beneficial in both pediatric and adult patients with uncontrolled seizures.

Lacosamide proved to be safe and beneficial in pediatric patients with uncontrolled seizures