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Long-term efficacy and safety of lacosamide monotherapy in the treatment of partial-onset seizures: A multicenter evaluation

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ABSTRACT

Purpose: The goal of this study is to report the efficacy and tolerability of lacosamide (LCM) monotherapy, as first-line and conversion regimens, in the treatment of patients with partial-onset seizures.
Methods: We retrospectively reviewed the charts of patients with focal epilepsy on LCM monotherapy from six centers in Spain. Efficacy and tolerability were evaluated in the overall group and in subgroups of patients who were naive to antiepileptic drug (AED) therapy (Group 1) and those who had previously been treated with AEDs (Group 2).
Results: Sixty-six patients were identified including 18 patients in Group 1 and 48 patients in Group 2. Patients were followed up for 0.5–54 months in monotherapy (mean 15.5 months). Forty-two (63.6%) patients remained seizure-free during all the follow-up. At 6 and 12 months, seizure-free rates were 77.6% and 72.3%, respectively. The drug was withdrawn in 10 (15%) patients (3 side effects, 6 lack of efficacy, 1 other reason). Fifteen (22.7%) patients reported mild to moderate side effects with the use of LCM. No differences were found between Groups 1 and 2 regarding efficacy outcomes or tolerability issues.
Conclusions: In our series more than two-thirds of the patients remained seizure-free on LCM monotherapy. Side effects were generally mild and led to discontinuation in only 3/66 (4.5%) patients. Our experience suggests that LCM monotherapy, either as first-line or after conversion, may be a valuable option for patients with focal epilepsy.

1. Introduction

Lacosamide (LCM) is an AED initially approved for the adjunctive treatment of partial-onset seizures in adult patients. Three double-blind, placebo-controlled trials [1–3] and two long-term follow-up studies [4,5] have established the clinical efficacy and safety of the oral formulation of LCM in patients with pharmacoresistant partial epilepsy. In 2014, a FDA license extension allowed LCM to be used as monotherapy for the treatment of partial-onset seizures in patients 17 years of age and older in the USA while in the European Union LCM has not yet received EMA approval for its use as monotherapy. A randomized, historical-controlled, monotherapy conversion trial conducted in the USA has demonstrated that LCM 400 mg/daily is effective for the treatment of adult patients with focal epilepsy with a favorable safety profile [6]. In Europe, a multicentre, randomized monotherapy study comparing LCM with sustained release CBZ in patients with partial-onset seizures is currently underway. So far, experience with LCM monotherapy in a real-life clinical setting is sparse and limited to reports of a few patients with conversion to monotherapy [4,7,8]. In the largest and more recent of these series,

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19 of 22 patients (86.4%) who were converted to monotherapy remained seizure free at 6 and 12 months follow-up [8]. However, no efficacy and tolerability data on the use of LCM as first-line monotherapy are available.

The aim of the present study is to explore the clinical outcome in patients on LCM monotherapy reached after initial prescription or after conversion to monotherapy in daily clinical practice.

2. Methods

All patients with partial onset-seizures from six hospitals in Spain who had been treated with at least one dose of LCM monotherapy since the introduction of the drug in September 2009 until May 2014 were identified. Charts were reviewed for patient demographic and clinical data including age at seizure onset, maintenance dose, duration of treatment and adverse events. For the purposes of this analysis patients were divided into two groups: those with recently diagnosed epilepsy for whom LCM was their first AED (Group 1) and those who reached LCM monotherapy after discontinuing other AEDs (Group 2). In the latter group we also recorded the reason for introducing LCM (seizure control or intolerance to other AEDs), and previous and concomitant antiepileptic drug therapy. After reviewing clinical data records, patients with an inaccurate diagnosis of epilepsy, treatment non-compliance and/or unreliable seizure frequency account were excluded from the analysis.

According to the participating physicians criteria, a daily dose of 50 or 100 mg of LCM was prescribed initially and titrated to an optimal maintenance dose for each patient depending on efficacy and tolerability.

Efficacy was evaluated by analyzing seizure-free rates and mean seizure frequency reduction during the complete follow-up and during the first 6 and 12 months after reaching the fixed maintenance dose. Seizure freedom was defined as no seizures on LCM monotherapy during the evaluated study period (complete follow-up or 6 and 12 months after reaching the maintenance dose).

Frequency and types of side effects related to the use of LCM were recorded. We also studied the one-year retention rate.

2.1. Statistical analysis

Data were analyzed using descriptive statistics. The Chi-square test (or Fisher's exact test if the expected frequency was lower than five in at least 20% of the cells) was used to compare subgroups with respect to efficacy, percentage of patients with AEs and discontinuation for AEs. The Mann–Whitney *U* test was used to analyze quantitative variables (time since epilepsy onset and number of seizures per month). Student's *t*-test was used to compare subgroups with respect to LCM dose changes.

Statistical significance was defined at $p < 0.05$. All statistical analysis was performed using SPSS version 19.0 (IBM Corporation, Armonk, NY, US).

3. Results

3.1. Patient population

We identified 66 patients with partial epilepsy who had received at least one dose of LCM monotherapy, 18 (27.3%) patients in Group 1 and 48 (72.7%) patients in Group 2. Only 2/66 patients had learning difficulties. Group 2 included 9 patients (13.6%) directly switched to LCM in the epilepsy monitoring unit or the emergency room and 39 (59.1%) patients slowly converted to LCM monotherapy. Mean number of prior AEDs in Group 2 was 2.41 (range 1–9, median 1) and 50% of the patients had previously tried 2 or more AEDs. Reasons for introduction of LCM in patients in Group 2 were seizure control in 29 (60.4%), tolerability problems in 10 (20.8%), both in 6 (12.5%), and treatment with an AED not considered to be appropriate for the type of epilepsy in 3 patients. The demographic and clinical characteristics of the patients are presented in Table 1.

Median monthly seizure frequency in the 12-month period prior to LCM monotherapy was 0.7 (SD 9.4; range 0–60) and mean follow-up in monotherapy was 15.5 months (range 0.5–54 months). Four patients had been seizure-free for at least one year previous to starting LCM. At the end of the study, 43 (65%) patients had received LCM monotherapy for more than 12 months.

Table 1
Patient demographics and characteristics.

Demographic and clinical data	Total population ($n=66$)	Group 1 ($n=18$)	Group 2 ($n=48$)
Female	37 (56%)	11 (61%)	20 (54%)
Mean age, years (range)	49.4 (16–92)	53.1 (18–90)	48 (16–92)
Mean ± SD age at epilepsy onset, years	42.9 ± 21.5	51.6 ± 23.5	39.6 ± 20
Mean ± SD time since epilepsy onset, years	6.5 ± 9.9	1.5 ± 2.1	8.4 ± 11
Etiology			
Symptomatic	35	10 (55.6%)	25 (52%)
Cryptogenic	31	8 (44.4%)	23 (48%)
Seizure type			
Simple partial	16	4 (22%)	12 (25%)
Complex partial	29	9 (50%)	20 (42%)
Secondarily generalized	39	11 (61%)	28 (58%)
Median (range) number of seizures			
3 month baseline period	2 (0–180)	1.5 (1–60)	2 (0–180)
12 month baseline period	3 (0–1080)	2.5 (1–60)	4 (0–1080)
Number of previous AEDs			
0	18 (27.3%)	18 (100%)	–
1	24 (36.4%)	–	24 (50%)
>2	24 (36.4%)	–	24 (50%)
Number of concomitant AED at baseline			
0	27 (40.9%)	18 (100%)	9 (18.7%)
1	34 (51.5%)	–	34 (70.8%)
2	5 (7.5%)	–	5 (10%)