Epilepsy Research (2015) 110, 115—118

journal homepage: www.elsevier.com/locate/epilepsyres

SHORT COMMUNICATION

# The effects of lacosamide on depression and anxiety in patients with epilepsy

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Received 23 September 2014; received in revised form 24 November 2014; accepted 2 December 2014
Available online 15 December 2014

**KEYWORDS**
Lacosamide;
Depression;
Anxiety;
NDDI-E;
GAD-7

**Summary** Depression and anxiety are common in patients with epilepsy. Moreover, some antiepileptic drugs (AEDs) have mood stabilizing and anxiolytic effects, while others may worsen psychiatric symptoms. The effects of lacosamide, a third generation AED approved for the treatment of focal onset seizures, on depressive and anxiety symptoms are unknown. We evaluated changes in depression and anxiety following the initiation of lacosamide. We compared patients' scores on the Neurological Disorders Depression Inventory for Epilepsy (NDDI-E, $n = 91$) and Generalized Anxiety Disorder 7-item (GAD-7, $n = 20$) scales prior to and following lacosamide treatment. Following the initiation of lacosamide, there were no significant changes in NDDI-E scores when all patients were analyzed aggregately (baseline: $12.14 \pm 4.64$ vs post-treatment: $11.91 \pm 4.14$, $p = 0.51$). Similarly, the mean GAD-7 scores at baseline ($4.10 \pm 4.52$) and after treatment ($4.75 \pm 5.51$) did not differ ($p = 0.23$). In the 25 patients with initial NDDI-E scores of >15, lacosamide was associated with a significant decrease in depressive symptoms (baseline: $17.60 \pm 1.63$ vs post-treatment: $14.64 \pm 2.78$, $p < 0.001$). NDDI-E and GAD-7 scores pre- and post-lacosamide initiation were not significantly affected by a history of mood disorders, concomitant psychiatric medications, or concomitant AEDs with mood-stabilizing effects.


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http://dx.doi.org/10.1016/j.eplepsyres.2014.12.007
0920-1211/

## Introduction

Two of the most common comorbidities in patients with epilepsy are depression and anxiety disorders. The prevalence of anxiety amongst patients with epilepsy ranges from 15 to 25%, while depressive disorders occur in 9—55% (Indaco et al., 1992; Robertson et al., 1994; Jacoby et al., 1996; Asadi-Pooya and Sperling, 2011). Such disorders have the potential to reduce quality of life as much as uncontrolled seizures and alarmingly increase the risk of suicidality (Pompili et al., 2006). Suicide may account for up to one third of deaths in patients with epilepsy (Pompili et al., 2006).

To screen for depression and anxiety in a clinical practice, neurologists often utilize screening tools, including the Neurological Disorders Depression Inventory for Epilepsy (NDDI-E) and Generalized Anxiety Disorder 7-item (GAD-7) scale. The NDDI-E is a 6 item self-rating instrument specifically designed to evaluate depression in people with epilepsy, with a maximum score of 24. A NDDI-E score of >15 has a specificity of 90%, a sensitivity of 81%, and a positive predictive value of 0.62 for detecting major depressive disorder (Gilliam et al., 2006). The GAD-7 scale is a 7-item instrument that measures anxiety symptoms (maximum score 21). It has good reliability, high sensitivity (89%) and very good specificity (82%) (Spitzer et al., 2006).

When tasked with addressing comorbid depression and/or anxiety in patients with epilepsy, neurologists may attempt to rely on potential mood stabilization properties of antiepileptic drugs (AEDs). Certain AEDs, such as carbamazepine, lamotrigine, oxcarbazepine, and valproate, are used to stabilize mood and/or treat bipolar depression (Eddy et al., 2012). Conversely, neurologists must be mindful of not exacerbating underlying psychiatric disorders with AEDs. These include levetiracetam and perampanel, both of which may contribute to increased anger, irritability, anxiety, and depression in some patients (Piedad et al., 2012; Rugg-Gunn, 2014).

Lacosamide (Vimpat®) was approved by the US Food and Drug Administration (FDA) for the adjunctive treatment of focal onset seizures in 2008 and as monotherapy in 2014. Although lacosamide is an effective treatment for focal onset seizures, its effects on mood remain largely unknown. While clinical trial data did not suggest adverse psychiatric effects, such studies did not utilize instruments to measure subtle changes in depression or anxiety (Ben-Menachem et al., 2007; Kelemen and Halasz, 2010). Accordingly, we sought to evaluate changes in depression and anxiety symptoms following the initiation of lacosamide in patients with epilepsy.

## Methods

### Study design

The electronic medical records of all patients evaluated at the University of Cincinnati (UC), Epilepsy Center from January 2008 to August 2012 were reviewed. Extracted data included seizure type, AEDs, concomitant psychotropic medications, history of mood disorder, and seizure counts. Concomitant AEDs were categorized as mood stabilizing (carbamazepine, oxcarbazepine, lamotrigine, and valproate) or not (all others).

Prior to the availability of lacosamide in October 2008, epileptologists at our institution administered the NDDI-E to patients at every initial and follow-up visit. The GAD-7 was not administered to patients at every visit until January 2011.

Subjects were selected for further review if they were: ≥18 years of age; were diagnosed with focal onset seizures; had lacosamide initiated following FDA approval; and had follow up at least once within 6 months of initiation of lacosamide treatment. For both the NDDI-E and GAD-7 analyses, subjects were required to have a minimum of 1 baseline NDDI-E/GAD-7 prior to initiation of lacosamide and at least 1 NDDI-E/GAD-7 following treatment initiation. Subjects were excluded from further analysis if they had cognitive impairment that rendered them unable to complete the NDDI-E and/or GAD-7, or if they discontinued lacosamide after <3 months.

### Statistical analysis

Paired *t*-test and Wilcoxon signed rank tests were used to compare the changes in NDDI-E and GAD-7 scores. The baseline NDDI-E and GAD-7, final visit NDDI-E and GAD-7, and change in NDDI-E and GAD-7 scores were separately compared based on histories of initial NDDI-E > 15, comorbid mood disorders, concomitant psychiatric medications, and mood stabilizing concomitant AEDs using unpaired *t*-tests and Wilcoxon rank sum tests. Univariate association of baseline cofactors on final NDDI-E and GAD-7 scores was examined using linear regression. Random intercept and random treatment effect mixed models were used to examine the effects of cofactors on NDDI-E and GAD-7 scores. *P*-values <0.05 were considered significant.

The protocol was approved by the UC Institutional Review Board. The clinical trial identifier number assigned by clinicaltrials.gov was NCT00526630.

## Results

### Demographics

Ninety-one patients were included in this study. See Table 1 for full demographic information. The majority of patients had comorbid mood disorders ($n = 62$, 68.13%) and/or received mood stabilizing concomitant AEDs ($n = 48$, 52.75%). A minority of patients were prescribed concomitant psychiatric medications ($n = 40$, 43.96%). NDDI-E scores were obtained before and after treatment in all patients ($n = 91$). However, only 20 patients had both pre and post-treatment GAD-7 scores available.

### Primary analyses

The mean baseline NDDI-E score was $12.14 \pm 4.64$; this was similar to the mean NDDI-E after treatment of $11.91 \pm 4.14$ (paired *t*-test $p = 0.51$; Wilcoxon signed rank test $p = 0.66$). The mean GAD-7 scores at baseline ($4.10 \pm 4.52$) and after