



# Levetiracetam Induced Acute Suicidal Ideations in a Patient of Juvenile Myoclonic Epilepsy

Ravikant Kumar<sup>1</sup>, Rahul Mathur<sup>2</sup>, Abhishek Chakladar<sup>3\*</sup>, Anuranjan Vishwakarma<sup>2</sup>

<sup>1</sup>Department of Psychiatry, National Drug Dependence Centre, All India Institute of Medical Sciences, New Delhi, India.

<sup>2</sup>Department of Psychiatry, All India Institute of Medical Sciences, New Delhi, India.

<sup>3</sup>Department of Psychiatry, Varun Arjun Medical College and Rohilkhand Hospital, Shahjahanpur, Uttar Pradesh, India.

## INTRODUCTION

The US Food and Drug Administration (FDA) approved levetiracetam as an antiepileptic drug (AED) in 1999. After nine years, the FDA released a post-marketing statement describing an increased risk of suicide (0.43%) in patients taking AEDs, including levetiracetam.<sup>1</sup> Levetiracetam is a second-generation AED that has shown clinical effectiveness in generalized and partial epilepsy syndromes as monotherapy and adjunctive treatment.<sup>2</sup> The recommended starting dose of levetiracetam is 500 mg twice daily and it can be titrated by 1,000 mg every 2 weeks as needed to a maximum dose of 3,000 mg daily.<sup>3</sup> The most common side effect of levetiracetam was found to be sedation at 10.7%, while mood disturbance was found in 4.8% of patients.<sup>4</sup> A possible association has been reported between the use of levetiracetam and suicidality.<sup>5</sup> We here describe the case of a patient with a history of juvenile myoclonic epilepsy without any family history or past history of psychiatric illness being treated with levetiracetam, who developed acute onset of suicidal ideations when the dose of levetiracetam was increased, which subsided in a span of five days when levetiracetam was gradually stopped and sodium valproate was introduced. To the best of our knowledge, this is one of the very few case reports from India that demonstrates the temporal association of levetiracetam with acute onset of suicidal ideations in the absence of other risk factors for AED-induced suicidal behavior.

## Case Report

Mr. S, 25 an old male from a Hindu nuclear family of middle socioeconomic status, presented to the neurology outpatient department with a history of seizure disorder. There was no family history or past history of any psychiatric illness. He was previously diagnosed as juvenile myoclonic epilepsy and was on levetiracetam 2 gm per day in divided doses on which he was maintaining seizure-free. There was no history of prior head injury and MRI scan of the brain was normal. The patient developed three episodes of breakthrough seizures (semiology suggestive of generalized seizures, witnessed by family members) on levetiracetam 2 gm in a span of seven days. Family members ensured com-

## ARTICLE INFO

### \*Correspondence:

Abhishek Chakladar  
avcal89@gmail.com

Department of  
Psychiatry, Varun Arjun  
Medical College and  
Rohilkhand Hospital,  
Shahjahanpur, Uttar  
Pradesh, India

### Dates:

Received: 28-09-2023

Accepted: 15-10-2023

Published: 08-11-2023

### How to Cite:

Kumar R, Mathur  
R, Chakladar A,  
Vishwakarma A.  
Levetiracetam Induced  
Acute Suicidal Ideations  
in a Patient of Juvenile  
Myoclonic Epilepsy.  
Indian Journal of  
Clinical Psychiatry.  
2023;3(2): 40-42.  
doi: 10.54169/ijocp.v3i02.94

© Authors, 2023. Open Access This article is licensed under a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International (CC BY-NC-SA 4.0) License, which allows users to download and share the article for non-commercial purposes, so long as the article is reproduced in the whole without changes, and the original authorship is acknowledged. If you remix, transform, or build upon the material, you must distribute your contributions under the same license as the original. If your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <https://creativecommons.org/licenses/by-nc-sa/4.0/>

pliance to medications. The consultant neurologist increased the dose of levetiracetam to 3 gms per day in a span of 2 weeks for better control of seizures. Three days after taking levetiracetam at 3 gms per day in divided doses, the patient started remaining irritable for most of the time during the day, developed anhedonia, easy fatigability, decreased appetite, decreased attention and concentration and pessimistic views about the future along with suicidal ideations. At this point, he was referred to the psychiatrist and he was admitted in view of active suicidal ideations. Hamilton Depression Rating Scale (HAM-D) and Hamilton Anxiety Rating Scale (HAM-A) were applied along with the Beck Scale for Suicidal Ideations (BSS) to estimate the severity of depression, associated anxiety, and suicidal ideations, respectively. The scores on HAM-D, HAM-A and BSS came out to be 22, 14 and 23, respectively, indicating mild anxiety and severe depressive episodes. Since the onset of suicidal ideations was temporally correlated with the escalation of the dose of levetiracetam, the drug was stopped and sodium valproate was introduced after consultation with a neurologist. In view of the severe depressive episode, escitalopram was started and maintained at 10 mg. Five days after levetiracetam was stopped, the suicidal ideations had decreased significantly, which correlated with a score of 5 on BSS. There was significant improvement in the mood and biological functions, which correlated with score of 12 on HDRS. On day 5 of stopping levetiracetam, the HAM-A score was 11. The patient was subsequently discharged on sodium valproate 1250 mg and escitalopram 10 mg and on follow-up he maintained seizure free on the same medications. There was no evidence of any mood symptoms during follow-up till 6 months, and escitalopram was tapered and stopped.

## DISCUSSION

Levetiracetam potentiates gamma-aminobutyric acid and modulate Ca<sup>++</sup> channels/K<sup>+</sup> currents and SV2A (a synaptic protein) involved in vesicle exocytosis.<sup>6</sup> Apart from sedation and mood symptoms, it is known to develop behavioral symptoms such as nervousness (3.8%), hostility (2.3%), anxiety (1.8%) and emotional lability (1.7%) in clinical trials.<sup>7</sup> These factors although could contribute to increased sui-

cidality, but none of them are directly associated. Levetiracetam can exert negative effects on mood and cognition due to lack of serotonergic properties.<sup>8</sup> Inhibition of glutamatergic neurotransmission by antiepileptic drugs has also been hypothesized as the pathophysiology of mood and behavioral disorders, but the effects of levetiracetam on the glutamatergic system still remain unknown.<sup>9</sup> The risk factors that contribute to suicidal behavior in patients with epilepsy on antiepileptic drugs (including levetiracetam) include temporal lobe epilepsy, surgically treated epilepsy, post-ictal psychosis, past and/or current history of mood and anxiety disorders, prior suicide attempts, family history of mood disorders complicated by suicide attempts and treatment-refractory epilepsy.<sup>10</sup>

Our case highlights the direct influence of levetiracetam on suicidality with the exclusion of seizure and comorbid psychiatric disorders. Our findings suggest the possibility that suicidality induced by levetiracetam was related to depression rather than anxiety. Suicidality and behavioural disturbances can be precipitated in patients on antiepileptic drugs, but this does not appear to have a “class effect”.<sup>5</sup> Although levetiracetam-induced psychiatric adverse effects are not considered to be dose related,<sup>11</sup> but this case suggests that rapid titration of dose may be an important factor in developing suicidal behavior. Larger prospective studies will be needed to further validate our findings. At this time, monitoring depressive symptom scales for patients taking antiepileptic drugs, especially levetiracetam seems to be beneficial.

## REFERENCES

1. Mula M, Bell GS, Sander JW. Suicidality in epilepsy and possible effects of antiepileptic drugs. *Curr Neurol Neurosci Rep.* 2010 Jul;10(4):327–32.
2. Surges R, Volynski KE, Walker MC. Is Levetiracetam Different from Other Antiepileptic Drugs? Levetiracetam and its Cellular Mechanism of Action in Epilepsy Revisited. *Ther Adv Neurol Disord.* 2008 Jul;1(1):13–24.
3. Betts T, Waegemans T, Crawford P. A multicentre, double-blind, randomized, parallel group study to evaluate the tolerability and efficacy of two oral doses of levetiracetam, 2000 mg daily and 4000 mg daily, without titration in patients with refractory epilepsy. *Seizure.* 2000 Mar;9(2):80–7.

4. Nicolson A, Lewis SA, Smith DF. A prospective analysis of the outcome of levetiracetam in clinical practice. *Neurology*. 2004 Aug 10;63(3):568–70.
5. Siamouli M, Samara M, Fountoulakis KN. Is antiepileptic-induced suicidality a data-based class effect or an exaggeration? A comment on the literature. *Harv Rev Psychiatry*. 2014;22(6):379–81.
6. Crepeau AZ, Treiman DM. Levetiracetam: a comprehensive review. *Expert Rev Neurother*. 2010 Feb;10(2):159–71.
7. Cramer JA, De Rue K, Devinsky O, Edrich P, Trimble MR. A systematic review of the behavioral effects of levetiracetam in adults with epilepsy, cognitive disorders, or an anxiety disorder during clinical trials. *Epilepsy Behav*. 2003 Apr;4(2):124–32.
8. Kalinin VV. Suicidality and Antiepileptic Drugs. *Drug-Safety*. 2007 Feb 1;30(2):123–42.
9. Perucca P, Mula M. Antiepileptic drug effects on mood and behavior: molecular targets. *Epilepsy Behav*. 2013 Mar;26(3):440–9.
10. Esang M, Santos MG, Ahmed S. Levetiracetam and Suicidality: A Case Report and Literature Review. *Prim Care Companion CNS Disord*. 2020 Jul 30;22(4):19nr02502.
11. Kaufman KR, Bisen V, Zimmerman A, Tobia A, Mani R, Wong S. Apparent dose-dependent levetiracetam-induced de novo major depression with suicidal behavior. *Epilepsy & Behavior Case Reports*. 2013 Jan 1;1:110-2.