

## Suicidality in epileptics on levetiracetam therapy with preceding comorbidity

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### Abstract

Anti-epileptic medications like levetiracetam, sodium valproate, topiramate and lamotrigine are known to produce serious adverse reactions like suicidal tendencies, Steven Johnson syndrome, toxic epidermal necrolysis, hepatic dysfunction, pancreatitis, depression and psychotic episodes. Here we report two patients who attempted suicide, had psychiatric comorbidity and alcoholism and were on treatment. One patient died and the other was treated for poisoning and survived.

Both the patients were on levetiracetam. It is assumed that levetiracetam could have contributed to the suicidal ideation as an adverse reaction. SUDEP (sudden unexplained death in epilepsy) might as well be considered in the second patient. It is suggested that patients on newer anti epileptics be screened for suicidal intent and treated for psychiatric comorbidity like depression. One of the patients had alcoholism and the other comorbid depression.

**Keywords:** Levetiracetam, Suicide, Epilepsy, Alcohol dependence, Sudep.

### The Case

#### Case 1

A 26 year old male with seizure semiology of generalized tonic clonic seizures with normal MRI and abnormal EEG had history of epilepsy for the last 3 years, who was on regular antiepileptic medication, He was initially on sodium valproate. Due to the adverse reaction in the form of gastric irritation and weight gain, he was started on levetiracetam monotherapy at a dose of 500mg twice daily. He was also on escitalopram at a dose of 10 mg for depression. Due to the development of breakthrough seizures, the dose was escalated to 750mg and later to 1000mg twice daily. The patient had good seizure control. He was under regular follow up in the Neurology outpatient clinic in a tertiary care teaching hospital. After a few months follow up, he reported with his parent with a history of suicide attempt with pesticide. He was immediately treated in a private hospital near his residence, with good recovery. He did not have seizures during the hospital stay. Currently he is on regular follow up.

#### Case 2

A 42 year old chronic alcoholic developed alcohol withdrawal seizures. He was admitted and treated with thiamine, chlordiazepoxide, ranitidine and levetiracetam. The dose of levetiracetam was 500mg twice a day, and later escalated to 1000mg twice a day due to recurrence of seizures. The patient on the fourth day fell from the fifth floor of the hospital and committed suicide which was assumed to be due to antiepileptic, levetiracetam. Whether he had a seizure before the fall was not documented by the witnesses.

### Discussion

Levetiracetam is a second generation antiepileptic agent. It has a broad spectrum antiepileptic activity for the treatment of all types of seizures. It binds to

synaptic vesicle protein 2A with a unique mechanism of action, which opposes excessive synchronized activity between neurons. It is primarily excreted renally. There are no reported drug interactions with other antiepileptic agents. Improvement in patient's quality of life has been considered as an advantage. Behavioral adverse effects have been reported. SUDEP (sudden unexplained death in epilepsy) in alcoholics have been reported in patients on levetiracetam.<sup>(1,2,3)</sup>

Suicidality is common in patients with epilepsy who are on the newer generation antiepileptic agents.<sup>(4,5,6)</sup> This phenomenon has been identified in patients who were on drugs like levetiracetam, lamotrigine and topiramate due to associated drug induced depression. Some patients were considered to have had SUDEP (sudden unexpected death in epilepsy).<sup>(9)</sup>

Suicide risk in epileptics are associated with substance use disorders particularly alcohol use in patients with depression. Certain genotypes like SSTR4 rs2567608 TT are vulnerable.<sup>(7)</sup> It has been suggested that all epilepsy patients and their families be informed about suicide and self-harm while on treatment with levetiracetam.

Certain groups of people who attempt suicide later develop epilepsy due to yet unknown common mechanism. Some risk factors<sup>(8)</sup> like early onset of seizures, increased seizure frequency, use of antiepileptic polytherapy, lack of aura before seizure, temporal lobe epilepsy, use of levetiracetam, psychiatric comorbidity, and use of antidepressants were identified in epilepsy patients who attempt suicide in this population of patients.

To conclude, patients and their families have to be made aware of suicidality to prevent epilepsy related mortality.<sup>(9)</sup> Coexisting comorbidity like depression and alcoholism need to be addressed to in patients who are treated with levetiracetam. Medical professionals and

caregivers of admitted patients have to be made aware of SUDEP in this patient population.<sup>(10)</sup>

## References

1. Weijenberg A, Brouwer OF, Callenbach PM. Levetiracetam Monotherapy in Children with Epilepsy: A Systematic Review. *CNS Drugs* 2015;29(5):371-82.
2. Lyseng-Williamson KA. Spotlight on levetiracetam in epilepsy. *CNS Drugs* 2011;25(10):901-5.
3. Tekgül H, Gencpinar P, Çavuşoğlu D, Dündar NO. The efficacy, tolerability and safety of levetiracetam therapy in a pediatric population. *Seizure* 2016;36:16-21.
4. Andersohn F, Schade R, Willich SN, Garbe E. Use of antiepileptic drugs in epilepsy and the risk of self-harm or suicidal behavior. *Neurology* 2010;75(4):335-40.
5. Mula M, Sander JW. Suicide and epilepsy: do antiepileptic drugs increase the risk? *Expert Opin Drug Saf* 2015;14(4):553-8.
6. 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.
7. Berent D, Emilien G, Podgórski M, Kusideł E, Kulczycka-Wojdala D, Szymańska B et al. SSTR4, Childhood Adversity, Self-efficacy and Suicide Risk in Alcoholics. *Transl Neurosci* 2017;8:76-86.
8. Nilsson L, Ahlbom A, Farahmand BY, Asberg M, Tomson T. Risk factors for suicide in epilepsy: a case control study. *Epilepsia* 2002;43(6):644-51.
9. Devinsky O, Spruill T, Thurman D, Friedman D. Recognizing and preventing epilepsy-related mortality. A call for action. *Neurology* 2016;86(8):779-86.
10. Devinsky O, Friedman D, Cheng JY, Moffatt E, Kim A, Tseng ZH. Underestimation of sudden deaths among patients with seizures and epilepsy. *Neurology* 2017;89(9):886-92.