Letter to the Editor

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Levetiracetam-Induced Acute Mania

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Dear Editor,

Levetiracetam is a novel second-generation antiepileptic agent with a good side-effect profile, used for the treatment of partial and generalized epilepsy[1]. Unlike other antiepileptic drugs, the action mechanisms of levetiracetam appear to involve neuronal binding to synaptic vesicle protein 2A, inhibiting calcium release from intra-neuronal stores, opposing the activity of negative modulators of GABA and glycine-gated currents and inhibiting the action of N-type calcium channels[2]. Levetiracetam, leading to an indirect enhancement of benzodiazepine GABA receptor function by removing the negative modulation of this site by zinc and beta carbolines or other GABAergic mechanisms, is also used rarely as an adjunctive mood stabilization agent for the treatment of both depressive and manic episodes of bipolar disorder with controversial results[3,4]. Central nervous system side effects such as behavioral symptoms (depression, hostility, agitation, emotional liability, anger, nervousness and depersonalization, and symptoms) may occur in up to 16% of patients receiving levetiracetam treatment[1,5]. Here, we aimed to attract the attention of clinicians and researchers to a patient presenting with manic symptoms probably triggered by levetiracetam treatment.

A 37-year-old female, without any prior personal or family history of psychiatric illness, was as inpatient to the Neurology Department under carbamazepine 800 mg/day and valproic acid 1250 mg/day treatment for uncontrolled epileptic seizures. Carbamazepine treatment was stopped; levetiracetam treatment was started and increased to 1000 mg/day. One week after initiation of the levetiracetam treatment; epileptic seizures were controlled, but symptoms including logorrhea, irritability, grandiosity, distractibility, decreased need for sleep, flight of ideas, and persecutory delusions developed. The patient was referred to the psychiatry department. According to DSM-5 (Diagnostic and Statistical Manuals of Mental Disorders Fifth Edition), substance/medication-induced bipolar and related disorder was diagnosed. She scored 31 on the Young Mania Rating Scale. Because of the developing manic symptoms, quetiapine 600 mg/day was added to the current medication. Blood valproic acid level was 116 microgram/mL. One week later, due to the continuation of the manic symptoms, quetiapine dosage was increased to 800 mg/day and oxcarbazepine 150 mg/day was added and increased to 300 mg/day. Symptoms such as flight of ideas, persecutory delusions and irritability decreased, but logorrhea, grandiosity and decreased need for sleep persisted. Levetiracetam was stopped. The treatment was adjusted to valproic acid 1000 mg/day, lamotrigine 150 mg/day and risperidone 2 mg/day. The manic symptoms and epileptic seizures gradually declined within a week.

According to our knowledge, this is the second case report of levetiracetam induced mania. Based on the chronology of events and was absence of concomitant medications that can precipitate mania, the possibility of levetiracetam-induced mania was high. Complete resolution of the patient's symptoms after discontinuation of

levetiracetam supports the hypothesis of this case report. The development of manic symptoms with antiepileptic treatment is unusual, because the prominent actions of these drugs on GABAergic mechanisms lead to mood stabilizing effects. We suggest that multiple effects of levetiracetam on neurons (especially opposing effects on GABA, glycine-gated currents and inhibiting the action of N-type calcium channels) might lead to behavioral disturbances including manic symptoms[2,3]. Clinicians should be aware of the unusual side effects of levetiracetam.

Keywords: *levetiracetam, mania, delusion*

References:

1. Park EM, Holmes JA, Reeder-Hayes KE. Acute mania associated with levetiracetam treatment. Psychosomatics 2014;55(1):98-100. **[CrossRef]**
2. Lyseng-Williamson KA. Levetiracetam: a review of its use in epilepsy. Drugs 2011;71(4):489-514.
3. Kruger S, Sarkar R, Pietsch R, Hasenclever D, Braunig P. Levetiracetam as monotherapy or add-on to valproate in the treatment of acute mania–a randomized open-label study. Psychopharmacology (Berl) 2008;198(2):297-9. **[CrossRef]**
4. Saricicek A, Maloney K, Muralidharan A, Ruf B, Blumberg HP, Sanacora G, et al. Levetiracetam in the management of bipolar depression: a randomized, double-blind, placebo-controlled trial. J Clin Psychiatry 2011;72(6):744-50. **[CrossRef]**
5. Dannaram S, Borra D, Pulluri M, Jindal P, Sharma A. Levetiracetam-induced acute psychotic episode. Innov Clin Neurosci 2012;9(10):10-2.

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