Depressive disorder following withdrawal pregabalin: A case report

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To the Editor

Pregabalin is a gamma-aminobutyric acid (GABA) analogue used in the treatment of fibromyalgia, diabetic peripheral neuropathy, neuropathic pain, partial seizure and various psychiatric disorders in clinical practice. It is thought to reduce calcium-dependent neurotransmitter release by binding to the alpha-2-delta part on voltage-gated calcium channels in the central nervous system[1]. In addition, its effectiveness of pain transmission is estimated to be via the noradrenergic and serotonergic pathways[2]. It was reported that pregabalin has a risk of addiction due to its mechanism of action, and its discontinuation may cause symptoms such as diarrhea, loss of appetite, agitation, mutism, self-mutilation, tachycardia, hypertension, tremor and suicide attempts[3,4]. There is a limited number of reported cases of pregabalin discontinuation in literature. There is a report showing that discontinuation of pregabalin may be associated with psychotic disorder[5], and a case report describing agitation findings[6]. However, to the best of our knowledge, there is no information in literature that pregabalin withdrawal may be associated with mood disorders. Presented in this report is the case of a 77 year old female patient using 225 mg of pregabalin per day due to myofascial pain who has developed depressive disorder after the sudden discontinuation of pregabalin.

A 77 year old female patient visited the psychiatry outpatient clinic with complaints of fatigue, weakness, boredom, loss of appetite and insomnia that started two months ago. In addition, weight loss, forgetfulness, loss of concentration, and psychomotor retardation were detected during examination. The patient was diagnosed with depressive disorder according to the DSM-V diagnostic criteria. Her 17-item Hamilton Depression Rating Scale (HAM-D) score was 42 and her Hamilton Anxiety Rating Scale (HAM-A) score was 26. The patient had no history of psychiatric illness, had known hypertension and congestive heart failure and had been using the same treatment for a long time. In addition, it was learned that the patient had been using 225 mg of pregabalin per day for 3 years due to being diagnosed with myofascial pain. Her physician suddenly stopped pregabalin treatment three weeks before the onset of her depressive complaints. Laboratory findings and neuroimaging such as brain MRI did not reveal any findings that could explain her current status. The patient's neurology, cardiology, endocrinology, and internal medicine consultations had no findings that could explain her depressive symptoms. Escitalopram 5 mg treatment was started and it was titrated to 10 mg within two weeks. During the 6 weeks of follow-up, the patient partially benefited from the treatment (HAM-D=36 and HAM-A=26). Mirtazapin 15 mg/day was added to the current treatment of the patient. The patient's complaints regressed during follow-up, the next month her HAM-D and HAM-A scores were 12 and 4, consecutively. The patient's six month follow-up revealed no recurrence of her complaints.

In this report, we are presenting an elderly patient who developed depressive symptoms after the sudden discontinuation of pregabalin. There is a limited number of reports of pregabalin discontinuation in literature. Regardless, even though pregabalin withdrawal has been associated with a wide spectrum—from anxiety disorder to psychotic disorder—to the best of our knowledge, there is no report indicating that it may be associated with depressive disorder[5-7]. Considering the temporal relationship between the withdrawal of pregabalin and the onset of depressive symptoms, we think that the most likely cause of depressive disorder in our patient is the sudden discontinuation of pregabalin.

Although the mechanism of the relationship between pregabalin withdrawal and depressive disorder is not fully elucidated, there are several possible mechanisms. Sudden withdrawal of chronic pregabalin use may have uncovered a pre-existing subclinical depression or may have caused depression in individuals who are susceptible to the stress of withdrawal[8]. On the other hand, abrupt discontinuation of pregabalin—a long term GABA precursor—may have increased GABA release as a rebound[1,2], Furthermore, the use of pregabalin, a substance with a mechanism of action similar to the long term benzodiazepine, may have caused damage to the 5-HT (serotonin) receptors. Therefore, it may play a role in the development of depression[8]. Finally, the sudden discontinuation of long-term pregabalin may have led to low stress tolerance and might have contributed to the development of depressive symptoms. In our case, the symptoms of depressive disorder partially benefited from escitalopram, a serotonin reuptake inhibitor, and benefited even more from mirtazapine, which is effective over a noradrenergic mechanism. This suggests that the depressive disorder associated with discontinuation of pregabalin may be due to a change in the noradrenergic mechanism.

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Although pregabalin is a drug that is frequently used in clinical practice and has a risk of addiction, there is limited literature information about the effects of its discontinuation. However, it is considered to be safe to decrease the dosage and stop pregabalin treatment[4]. Furthermore, due to an increase of pregabalin prescriptions, the management of patients is gaining importance. In addition, the use of pregabalin and recognition of withdrawal symptoms by clinicians will facilitate the management of patients. We suggest that future studies should be directed towards preventive and appropriate supportive therapies for the management of acute pregabalin withdrawal.

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References

1. Taylor CP, Angelotti T, Fauman E. Pharmacology and mechanism of action of pregabalin: the calcium channel α2–δ (alpha2–delta) subunit as a target for antiepileptic drug discovery. Epilepsy Res. 2007;73:137-150.
2. Solutions M. Truven Health Analytics, Inc. Ann Arbor, MI www. micromedexsolutions.com Accessed May 2018; 8.
3. Barrett JA, Kittler LM, Singarajah C. Acute pregabalin withdrawal: A case report and review of the literature Southwest J Pulm Crit Care. 2015;10:306.
4. Yargic I, Ozdemiroglu FA. Pregabalin abuse: a case report. Klinik Psikofarmakol Bulteni. 2011;21:64-66.
5. Gundogmus İ, Karagöz A, Algül A. First-episode psychosis induced by pregabalin withdrawal: a case report. Psychiatry and Clinical Psychopharmacology 2018; 28: 461-463.
6. Barrett J, Kittler L and Singarajah C. Acute pregabalin withdrawal: a case report and review of the literature. Southwest J Pulm Crit Care. 2015;10:306-310.
7. Naveed S, Faquih AE, Chaudhary AMD. Pregabalin-associated discontinuation symptoms: A case report. Cureus. 10(10):e3425.
8. Olajide D, Lader M. Depression following withdrawal from long-term benzodiazepine use: a report of four cases. Psychol Med. 1984;14:937-940.