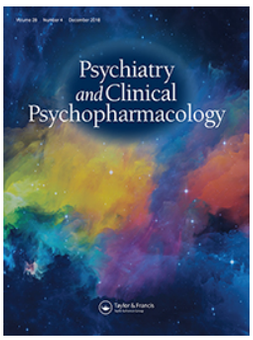

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CASE REPORT

First-episode psychosis induced by pregabalin withdrawal: a case report

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ABSTRACT

Pregabalin is a novel isomer of gamma-aminobutyric acid that functions as a major inhibitory neurotransmitter in the brain. It is used daily in medical practice for treating neuropathic pain, fibromyalgia, generalized anxiety disorder, and partial seizures. Due to its anti-glutamatergic effects, it poses a potential addiction risk. For example, an abrupt discontinuation of this substance may cause patients to exhibit physical withdrawal symptoms, such as insomnia, nausea, headache, and diarrhoea. However, there is no information in the literature that addresses whether the rapid discontinuation of pregabalin can cause psychosis to occur. Here we presented a 20-year-old patient with his first episode of psychosis that was likely attributable to his withdrawal from a high dosage pregabalin. He lacked physical signs of withdrawal; however, a psychiatric examination was conducted. It was determined that the patient was experiencing paranoid ideation, auditory hallucinations, and mutism. Furthermore, he had engaged in self-mutilative actions and had attempted suicide. Due to the short time frame between the rapid discontinuation of a relatively large dose of pregabalin and the onset of the patient's first episode of psychosis, it is likely that the psychotic episode was triggered by the cessation of the medication. This is the first known case of psychosis that was caused by the rapid withdrawal of pregabalin to be discussed in the literature. The results of this clinical case may guide clinicians to recognize the symptoms of acute pregabalin withdrawal.

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KEYWORDS
Pregabalin; psychosis; withdrawal

Introduction

Pregabalin is a novel isomer of gamma-aminobutyric acid (GABA) that functions as a major inhibitory neurotransmitter in the brain. It is used daily in medical practice for treating neuropathic pain, fibromyalgia, generalized anxiety disorder, and partial seizures [1]. Pregabalin is known for its ability to bind to the α2-δ subunit of voltage-gated calcium channels in various regions of the central nervous system. Additionally, pregabalin reduces the release of some neurotransmitters, such as glutamate, noradrenaline, serotonin, dopamine, and substance P [1,2]. Although pregabalin is known to be a safe, effective, and well-tolerated medication, tolerable side effects such as dizziness and somnolence have been documented [3]. Pregabalin, which is a GABA analogue similar to alcohol and benzodiazepines, is associated with a potential for dependence and a potential addiction risk due to its anti-glutamatergic effects [4]. Although there is no clear information about the tolerance to the effect of pain, it is known that pregabalin has a lower potential for addiction than that of benzodiazepines [5]. Nevertheless, studies have shown that the abrupt discontinuation of pregabalin may lead to withdrawal symptoms that are suggestive of physical dependence, such as insomnia, nausea, headache, and diarrhoea [6]. However, this is the first known case to address whether a patient's first occurrence of psychosis may be attributable to their rapid discontinuation of pregabalin.

This case focused on a patient who was experiencing his first episode of psychosis that was likely due to his withdrawal from a high dosage of pregabalin. After a psychiatric examination, the patient exhibited signs of withdrawal that included paranoid ideation, auditory hallucinations, and mutism. Further, he had engaged in self-mutilative actions and had attempted suicide.

Case report

Mr V is a 20-year-old male, engaged, primary school graduate with no past psychiatric history. In May 2017, he was referred for the first time to the outpatient clinic. It was his fifth day of military service. From the patient's detailed history, it was learned that he had a prison history, was a non-smoker, and had no history of alcohol or substance abuse. However, he had been taking pregabalin for pain in the amount of 2.7 g/day (9 capsules × 300 mg) for the past year. He presented to the clinic with paranoid ideation, auditory hallucinations, and mutism. Additionally, he had engaged in self-mutilative actions and had attempted suicide.

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The patient was assessed according to the Diagnostic and Statistical Manual (DSM-5); he received a SAPS score of 47 and a SANS score of 59. As a result, he was diagnosed with his first psychotic episode. After receiving the diagnosis, he was hospitalized and medicated with olanzapine, which was administered orally in the amount of 20 mg/day. The patient stated that he had stopped taking pregabalin five days before applying for psychiatric services, and that his complaints began on the third day after this cessation. On the fourth day after stopping his use of pregabalin, his psychotic symptoms escalated. He reported that he did not want to speak with anyone and that he thought people were talking about him behind his back. Further, he complained that he believed that people would hurt him, which caused him to become physically aggressive with others. He also injured himself with a cutting tool and attempted to commit suicide attitude by jumping from a high place. Before he stopped treating with pregabalin, neither he nor his family had any such complaints.

A psychiatric examination that was compatible with the patient's age was conducted. The examination found that the patient had poor self-care, slowed psychomotor activity, and disorganized behaviour. Further, the patient was diagnosed with having a dysphoric mood disorder and a blunted affect. He was also experiencing visual and auditory hallucinations; however, there were no signs that the patient was experiencing depersonalization-derealization disorder. Additionally, the examination found that the patient was experiencing impoverished thought content, decreased speed of thought, and loose associations. An EEG, a brain MR, laboratory tests, and a neurology consultation were conducted. The results were within normal limits.

Seven days after beginning treatment with olanzapine, the patient's complaints began to diminish. At that time, he was reassessed according to the DSM-5; he received a SAPS score of 36 and a SANS score of 45. On the 20th day, the patient's complaints had largely declined. Again, he was assessed according to the DSM-5 and received SAPS and SANS scores of 15 and 18, respectively. After receiving these scores, it was determined that the patient had entered remission. During his first month of olanzapine treatment, the patient did not experience any further psychotic symptoms. After treating with olanzapine for six months, the patient reported that he had no further psychiatric complaints.

Discussion

This case focused on a patient who developed his first psychotic episode after he rapidly discontinued taking a relatively large dose of pregabalin. After receiving antipsychotic treatment, his symptoms were reduced within three weeks and did not reoccur. The examination, brain MR, EEG, and laboratory tests did not offer any alternative explanations for the cause of his symptoms. Because of the close temporal relationship between patient's rapid discontinuation of a relatively large dose of pregabalin, the onset of his symptoms, and the singularity of his psychotic episode, it is probable that pregabalin played a causative role in the patient's psychosis. This is the first known case of psychosis that was caused by the rapid withdrawal of pregabalin to be discussed in the literature.

Numerous studies on the pathophysiology of psychosis have shown that the GABA receptor complex is a key factor in dopaminergic neurotransmission within the central nervous system. When GABA hypofunction is present, or when there are a reduced number of GABA neurotransmitters in the central nervous system (including the hippocampus, prefrontal cortex, and the limbic cortical and subcortical regions), cognitive impairments can occur. These cognitive impairments may include poor affect regulation, memory deficits, and positive symptoms of psychosis, including hallucinations [7–9]. Like benzodiazepine, pregabalin may benefit patients who have been diagnosed with psychosis due to its GABAergic effect. It is still unclear how the rapid withdrawal of pregabalin can cause psychosis; however, when a patient has built a tolerance to a relatively large dose of pregabalin and then rapidly withdraws from the medication, a temporary increase in dopaminergic, serotonergic, and noradrenergic activity in some parts of the central nervous system, including the limbic system, may occur. This may potentially lead to a temporary psychotic experience and may explain the pathophysiology that occurs in this case. Although there is no literature on pregabalin-induced psychosis, there are documented cases of psychosis caused by a patient's withdrawal from benzodiazepines that have GABAergic activity [10,11].

Finally, although pregabalin is widely used as a treatment for various diseases and psychiatric disorders, it also has the potential to be addictive. This is likely due to its euphoric and dissociative effects that are like those caused by benzodiazepines and alcohol. Additionally, because pregabalin can be used to treat a variety of different diseases and disorders, the substance may be relatively accessible to patients who have become addicted to the drug. As with any addictive substance, clinicians should be aware of the symptoms of overuse and withdrawal of pregabalin. In this case, a 20-year-old male patient began to exhibit psychotic symptoms three days after he suddenly ceased taking his pregabalin medication, which he had been taking in the amount of 2.7 g/day for one year.

Conclusion

Clinicians should be taught to recognize the symptoms caused by acute pregabalin withdrawal. When it is no

longer necessary for a patient to continue using pregabalin, the amount they are taking should be reduced and then eventually stopped, especially for a patient with pregabalin dependence or abuse. Also, clinicians should exercise caution when prescribing pregabalin to people who may potentially become addicted to the medication. Further studies are needed to clarify the precise mechanism that causes psychosis induced by pregabalin withdrawal.

Disclosure statement

No potential conflict of interest was reported by the authors.

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