Pregabalin Dependence: A Case Report

Pregabalin Bağımlılığı: Bir Olgu Sunumu

Gülay Oğuz[1], F. Mükerrem Güven[2], Sedat Batmaz[3]

ABSTRACT

Pregabalin is a new generation antiepileptic drug that exerts its effects by decreasing the release of neurotransmitters, such as glutamate, noradrenaline, and substance P. Pregabalin is a gamma-aminobutyricacid (GABA) analogue utilized in the treatment of neuropathic pain and generalized anxiety disorder, in addition to epilepsy. There have been studies conducted in recent years demonstrating the effectiveness of Pregabalin in the treatment of benzodiazepine and alcohol dependence. However, there have also been cases in which pregabalin dependence developed. As such, pregabalin should be used with caution. This article presents a case report of a 27-year-old man who started on pregabalin in order to discontinue synthetic marijuana (Jamaica) use, then abused it and exhibited withdrawal symptoms when not using it. The patient had been taking 2100 mg/day of pregabalin, and stated that he experienced withdrawal symptoms including irritability, shaking, heartburn, inertia, depression, and an inability to work when he hadn't taken the medicine. His daily dose of pregabalin was decreased according to a provided chart and he was started on paroxetine at 20 mg/day, and quetiapine XR at 50 mg/day. Following this intervention, the patient managed to quit pregabalin within 60 days.

Key Words: GABA, pregabalin, substance dependence.

ÖZET

Pregabalin glutamat, noradrenalin ve P maddesi gibi nörotransmitterlerin salınımını azaltarak etki eden yeni kuşak bir antiepileptiktir. Epilepsi dışında nöropatik ağrı ve yaygın anksiyete bozukluğunun tedavilerinde kullanılan bir gama-aminobutirikasit (GABA) analoğudur. Son yıllarda benzodiazepin ve alkol bağımlılığı tedavisinde etkili olduğunu gösteren çalışmalar vardır. Bu arada pregabaline bağlı birkaç bağımlılık gelişen vaka saptanmış olup bu nedenle pregabalin kullanımı sırasında dikkatli olmak gerekir. Bu yazıda Sentetik Esrar (Jamaica) kullanımı kesmek amacı ile pregabalin kötüye kullanımı gelişen ve yoksunluk belirtileri gösteren bir erkek hasta sunulmuştur. 2100 mg/gün pregabalin kullanan hasta ilaç almadığı zamanlarda sinirlilik, titreme, mide yanması, durgunluk, isteksizlik, çalışamama gibi yoksunlık belirtileri gösteriyordu. Pregabalin dozu bir çizelge düzenlenerek azaltıldı ve paroksetin 20 mg/gün, ketiyapin XR 50 mg/gün başlandı. Bu kombinasyonla hastanın pregabalin kullanımı 60 günde sonlandırıldı.

Anahtar Kelimeler: GABA, madde bağımlılığı, pregabalin.

[1] Yrd. Doç. Dr., Canik Başarı Üniversitesi, Fen Edebiyat Fakültesi, Psikoloji Bölümü
[2] Uzm. Dr., Özel Lara Anadolu Hastanesi
[3] Yrd. Doç. Dr., Gaziosmanpaşa Üniversitesi, Tıp Fakültesi, Ruh Sağlığı ve Hastalıkları Anabilim Dalı

Address reprint requests to:
Gülay Oğuz; Canik Başarı Üniversitesi, Fen Edebiyat Fakültesi, Psikoloji Bölümü, Samsun - TURKEY

E-mail address:
gozdemir24@hotmail.com

Phone:
+90 (362) 432 35 35

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INTRODUCTION

Pregabalin is a structural analogue of γ-aminobutyricacid (GABA). It is a ligand that exerts anticonvulsant, analgesic, and anxiolytic effects in animal models and has a high affinity for α-2-δ subunits of voltage-sensitive calcium channels (VGCC) (1). After forming a strong bond with the α-2-δ subunit of calcium channels of hyperexcited neurons, it decreases depolarization-induced calcium influx, thereby reducing the emissions of numerous excitatory neurotransmitters, including glutamate, noradrenaline, and substance P. Pregabalin was found to be superior to placebo in a double-blind, placebo-controlled study conducted on 344 patients with generalized anxiety disorder (GAD) (2). Pregabalin was also found to be superior to placebo in two more studies, and equivalent to lorazepam and alprazolam in two other studies, in terms of effectiveness for GAD (3-5). Pregabalin has also been used for the treatment of benzodiazepine dependence and withdrawal, as well as relapse prevention in alcohol dependence (6-7).

Despite the broad range of utilization of pregabalin, the number of case reports on its abuse potential and dependence has recently increased (8-22). For example, it has been reported that controlled clinical studies carried out in over 5500 patients demonstrated that 4 % of pregabalin-treated patients versus 1 % of placebo-treated patients developed abuse. The abrupt or rapid discontinuation of pregabalin has also been associated with insomnia, nausea, headache, or diarrhea, all of which could be suggestive symptoms of physical dependence (16, 18). These reports highlight the need for a closer follow-up in patients who have been prescribed pregabalin for a variety of psychiatric and/or neurologic disorders. Reports have also emphasized the complex relationship between pregabalin and previous drug abuse. This report aims to provide another case of pregabalin dependence in a patient with previous history of drug use, who was successfully treated.

THE CASE

Presenting Problem and History

Mr. Ö., a 27-year-old, married salesman presented to the psychiatry outpatient department for treatment to discontinue pregabalin use. At the time of presentation, the patient was using 2100 mg/day pregabalin in addition to marijuana and alcohol. A detailed history of his past substance use revealed that he first started using opioid drugs when he was 17 years old and later started to abuse alcohol as well. When he was 25 years old, he started using synthetic marijuana (Jamaica), which continued for eight months. The patient stated that his life changed entirely after using it, that he became extremely angry if he did not take it, and that he consequently increased the dose gradually. The patient, who eventually became unable to work, managed to quit the opioids on his own 14 months prior to his hospital visit. Since he suffered from extreme withdrawal symptoms during this period, he began taking pregabalin at the suggestion of a friend. He started with 300 mg/day pregabalin then eventually increased the dose up to 2100 mg/day.

The patient reported that he felt cheerful, extremely strong, and happy while using pregabalin, but that he suffered from trembling, sweating, and muscle pains when he was unable to obtain it. Other problems he had while not using it were irritability, insomnia, loss of appetite, heartburn, inertia, a desire to be away from people, and inability to go to work; he therefore did not want to quit using it. He could not handle being off of pregabalin for more than 2 days. The patient was able to obtain pregabalin without a prescription from pharmacies until 2013, then found illegal means of obtaining it. He stated that he decided to get help because of his daughter and that he was worried that he would not be able to work ever again if he continued his life in this way.

Mental State Examination

The patient, who had taken pregabalin only one day prior to presenting at the psychiatric clinic, was considered open to communication, and showed signs of adequate self-care. It was observed that he had depressive symptoms and impulsive personality features. His Beck Depression Inventory score was 30/63, and his Beck Anxiety Inventory score was 45/63. No significant results were observed in the blood tests conducted. The patient was diagnosed with alcohol and substance abuse disorder, generalized anxiety disorder, and sedative, hypnotic or anxiolytic use disorder (due to the use of pregabalin),

according to the Diagnostic and Statistical Manual of Mental Disorders (DSM) 5 criteria (23). The patient's urine toxicology screen was negative since he had not used any substances for a long time.

Follow-up Period

During the follow-up period, the patient's pregabalin dose was reduced to 900 mg twice daily. 20 mg of paroxetine and 50 mg of quetiapine were also prescribed, and pregabalin was gradually reduced over a period of 60 days, at which point it was discontinued altogether. During the cross-tapering period, the paroxetine dose was increased up to 40 mg/day, and the quetiapine dose raised to 150 mg/day. At the same time, psychotherapeutic interventions employing cognitive behavioral therapy techniques focusing on anger management issues, stress management, overcoming anxiety and depression, and coping strategies for withdrawal symptoms were commenced. Two weeks after the cessation of pregabalin, his BDI score had decreased to 12/63, and the BAI score was 15/63. All urine toxicology screening tests remained negative throughout the treatment. The patient's psychotherapy sessions continued bimonthly for four months, then monthly for two more months. The patient has been in remission since his last visit.

DISCUSSION

Ethanol, benzodiazepines, and some anticonvulsant medications affect GABA receptors directly, causing them to exert anxiolytic, sedative/hypnotic, and anticonvulsant effects. Pregabalin is prescribed 150-450 mg/day for alcohol dependence, and 225-900 mg/day for benzodiazepine dependence. Pregabalin is also known to be useful in treating generalized anxiety disorder, particularly in cases with opioid drug addiction. There are also case reports mentioning that it provides relief of symptoms due to benzodiazepine withdrawal (6). In addition, in a placebo-controlled study in the same disease group, pregabalin was shown to be superior to placebo in the alleviation of benzodiazepine withdrawal syndrome, albeit not statistically significant (24). In a review conducted on its use for alcohol dependence, a 150-450 mg/day dose of pregabalin for alcohol withdrawal symptoms showed conflicting results. According to the database of the German Federal Institute for Drugs and Medical Devices (BfArM), as of September 2012 there were fifty-five case reports related to pregabalin in relapse prevention; 44 of them were cases of dependence while the remaining cases were pregabalin abusers. Mean pregabalin doses used were reported to be between 400 mg/day and 6000 mg/day. Twenty-two of the 35 patients with available information had a coexisting different psychotropic substance abuse/addiction, while 27 patients had history of a different psychotropic substance abuse/addiction in the past (14). Pregabalin has been found to be effective in reducing dependence symptoms, but abuse of pregabalin has developed in some patients (14). The presence of a previous drug and/or alcohol abuse/dependence history seems to be a shared characteristic in cases where dependence to pregabalin develops. Other noteworthy comorbidities in such patients might include anxiety disorders, personality disorders, and possible mood disorders. The present case also had a history of drug use, and elevated scores on the depression and anxiety scales, with features suggestive of a personality disorder, all in line with previously published case reports in the literature.

Although pregabalin has a low dependence propensity, it poses a risk due to its euphoria effect (8, 10, 14). The euphoria effect of pregabalin (1-10 %) is experienced by more patients compared to placebo (0.5 %). There are also some studies on pregabalin dependence in the literature (7-11). However, research has failed to show that pregabalin is active at receptor sites associated with drug abuse. Its precise mechanism of action in the area of nucleus accumbens is also yet to be identified (18). The reward effect of pregabalin has been implicated in its potential for abuse (8).

Although it has been shown that pregabalin is effective in the treatment of some psychiatric disorders, in addition to epilepsy, it should be used with caution, particularly in patients with alcohol or drug addiction.

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