CASE REPORT

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Two Cases with Pregabalin Abuse: Relieving the Pain

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ABSTRACT Pregabalin is a gamma-aminobutyric acid analog which binds to the alpha 2-delta subunit of voltage-dependent calcium channels. Pregabalin is licensed for epilepsy, neuropathic pain, fibromyalgia and generalized anxiety disorder worldwide. However, as the pregabalin has become more prescribed, there has been increasing trend of pregabalin abuse. In this case series, we reported a 25-year-old male and 37-year-old women presenting to the outpatient addiction clinic with daily pregabalin abuse. Both patients had pain complaints secondary to neurological disorders and discovered the drug's relieving effects while abusing. A standard treatment protocol (duloxetine and diazepam) was started. During the follow-up, women patient stopped pregabalin. However, the male patient dropped out. The current case series suggest that prescribed drugs might cause tolerance, withdrawal, craving and repetitive use even when it causes problems. Prescribers and addiction specialists should have increased awareness concerning the abuse potential of pregabalin.

Keywords: Pregabalin; abuse; pain; case

Pregabalin is indicated for the treatment of epilepsy and neuropathic pain. The drug is a known inhibitor of α2γ-subunit of voltage-dependent calcium channels which inhibites calcium entry into neurons resulting in decrease of neuronal excitability.[1,2]

Despite the restrictions on the use of the drug which was classified as controlled substance, there has been a dramatic increase in pregabalin use, abuse, poisonings and deaths in many countries. Based on a 2013 UK study, lifetime prevalence within the general population is estimated at 2.5%. Pregabalin can produce desirable effects alone but is often used concomitantly with other drugs.[3-5] Pregabalin abuse rates within populations with substance use disorder (particularly opioid use disorder) are much higher (3-68%). Regarding reasons underlying pregabalin abuse, majority of the studies reported: 1) "liking", euphoric high subjective feeling 2) self-treatment of a variety of substance-related or medical conditions 3) potentiating the effects of substances.[6]

Euphoria is reported to be a dose-dependent adverse effect of pregabalin. In line with this finding, the high amounts of pregabalin consumption were reported in previous case reports (maximum daily doses of 800-12,000 mg/day).[6,7] The abrupt or rapid discontinuation of the drug has been associated with a variety of symptoms all of which might be suggesting physical dependence.[8]

This report aims to increase awareness concerning the use of pregabalin in patients with substance use history and self-treatment motivation of back-pain.

The author obtained written informed consents from the patients prior to publication.

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CASE REPORTS

CASE 1

A 25-year-old married male presented to the outpatient treatment clinic (OTC) with complaints of regular pregabalin use. Four years ago, after falling down from the stairs, patient's lower back pain started. He had used non-steroidal anti-inflammatory drugs (NSAID), naproxen and tenoxicam for 6 months. He stopped the medication due to insufficient improvement in the pain. He reported using cannabis, ecstasy and methamphetamine several times but did not use regularly. The last drug used was methamphetamine, 3 years ago.

30 months ago, he started using pregabalin by obtaining from a friend. He continued to obtain 300 mg once in two day or daily for 18 months. He perceived improvement in his pain. He also felt energetic, happy and reckless. Given that he was not getting the same effect, he increased the dose 1 year ago. Over the course of the last year, the patient gradually increased the dosage to 4,500 mg/day. 9 months ago, he applied to a specialized psychiatry center to try stopping pregabalin. He was prescribed sertraline 50 mg/day, but he discontinued the drug after taking "one or two tablet" due to sedation.

The patient reported that he suffered from inertia, insomnia, loss of appetite, restlessness, dysphoria and eye-redness when he was unable to obtain it. He decreased the dose down to 1,800 mg/day within the last month. He obtained the drug on the black market since the beginning. He decided to get help because he felt worried that he would be dependent on pregabalin "forever".

His physical examination, routine blood tests and toxicology screening were within normal limits. The family history was not significant. 600 mg of pregabalin treatment was prescribed for the patient, with a plan to taper the dosage by 150 mg each week, ultimately discontinuing the treatment over a period of 4 weeks. He was prescribed duloxetine 30 mg/day which was planned to be increased up to 60 mg/day in 10 days and diazepam 20 mg per day. The patient dropped out the treatment.

CASE 2

A 37-year old divorced woman visited the OTC, complaining of regular pregabalin use. She started using pregabalin 4 years ago after chronic lower back pain. She was diagnosed with lumbar hernia and prescribed NSAIDs (meloxicam and etodolac). Since NSAIDs were inefficient, patient was prescribed 75 mg pregabalin bid for chronic pain. Within two months she gradually increased the dosage up to 300 mg without medical supervision. After she perceived improvement in her pain, she continued obtaining. She also felt euphoric, relaxed and reckless. To get the same effect, she kept increasing and eventually was consuming 2,400 mg/day for the last 6 months. At this dose, she had increased work performance, increased appetite and felt euphoric.

However, she started to experience fatigue and insomnia lately possibly due to tolerance. Whenever she tried to discontinue pregabalin, she experienced withdrawal symptoms including irritability, craving, decreased appetite, lack of self-confidence, insomnia and social withdrawal.

She reported using methamphetamine once a week for 2 months in her adolescence period. She had a history of intimate partner violence in the past by his boyfriend. She felt depressed and had fatigue nearly every day, markedly diminished interest in activities, concentration problems and feelings of worthlessness during these years. Thus she was started on 50 mg/day sertraline medication. She stopped the medication after 4 weeks due to sedation.

During psychiatric examination, she was depressive and anergic with insomnia. She was with poor appetite lately. Her physical examination, routine blood tests and toxicology screening were within normal limits. The family history was not significant. She had stopped taking pregabalin a week ago. She was prescribed duloxetine 30 mg/day which was planned to be increased up to 60 mg/day in 10 days and diazepam 20 mg/day for 4 weeks. Diazepam treatment was stopped across the subsequent 4 week period with a plan to taper the dosage by 5 mg each week. Six months from the cessation of pregabalin, her mood was euthymic and she remained abstinent.

DISCUSSION

In this case series, we present two patients mostly identical to each other with the diagnosis of pregabalin use disorder who discovered pregabalin to relieve back pain but started to abuse it.

The need to alleviate back pain in our cases might contribute to pregabalin abuse. We used duloxetine to treat depressive symptoms in addition to analgesic effect. Benzodiazepine, diazepam, was used to alleviate restlessness and anxiety symptoms. The patients that we described used higher pregabalin doses than therapeutic doses (2,500 and 4,500 mg). Patients reported pleasant stimulation and euphoria when using supratherapeutic (1,500-12,000 mg) pregabalin dosages.[6,8,9] The occurrence of euphoric mood might be the key factor leading some patients, especially those without substance use history, to ingest large doses of pregabalin.[10,11]

A population-based study identified younger age, male sex, number of prescribers, diagnosis of cancer, neuropathy, depression and previous substance use as risk factors for gabapentinoid misuse.[12] In line with this study, our cases had substance use experience and depressive symptoms in the past. A study from Israel investigating pregabalin misuse motives in patients with substance use disorders reported that the most prevalent reason for its use was "analgesia" (45.8%). Interestingly one would think that patients with substance use disorder may choose pregabalin as a recreational substance. However motives to seek the euphoria reported in only a minority of those (%13.9).[13] Therefore it is not surprising that our patients' motive was relieving the pain.

Recent qualitative interviews of individuals abusing pregabalin revealed euphoria and improved sociability were the most common non-therapeutic effects desired; activating, sedating, dissociative or amnesiac effects were also noted.[14] In our cases, patient were euphoric, socially and physically active while using the drug.

Physical dependence and withdrawal have also been widely reported. Among patients in a German detoxification facility using pregabalin, those using pregabalin non-therapeutically described social phobia, fear, suicidal thoughts, sexual dysfunction or withdrawal symptoms including "exhaustion, headaches, anxiety, depression, insomnia, sweating and avoiding social interaction".[15] In line with literature, our cases reported withdrawal symptoms after cessation of the drug.

Evidence suggests that pregabalin misuse represents a trend to grow and cause significant patient harm. Although it was restricted by insurance providers to reach drugs that might be misused such as pregabalin, there could still be lack of adequate risk assessment among clinicians. Particularly, it is crucial to identify individuals at risk of misuse among patients undergoing pregabalin treatment primarily for its analgesic properties, especially in cases of neuropathic pain. Prescribers and addiction specialists should monitor alarming signs with high-risk groups, particularly those with concomitant substance use or substance use history. Those individuals with high-risk should be referred to substance use treatment centers where the integrated drug misuse treatments might be provided.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

This study is entirely author's own work and no other author contribution.

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