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CASE REPORT

Psychotic symptoms during phenibut (beta-phenyl-gamma-aminobutyric acid) withdrawal

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Abstract
Background: Phenibut is a GABAB agonist that was developed in the Soviet Union in the 1960s. In Russia, it is used in clinical practice to treat, for example, anxiety and alcohol withdrawal symptoms. In Europe and in the United States, phenibut is marketed as a nutritional supplement for improved sleep. In different Internet discussion forums, there are several reports of withdrawal symptoms. Aim: Our aim was to share what we have learnt from a case study wherein a patient was followed throughout the whole abstinence period.
Case report: A somatically healthy man in his mid-20s with a previous history of substance abuse took phenibut for 2 months. He noted tolerance development already after the first week and increased doses up to 20 g/day. Already a few hours after the last dose the patient started to experience subjective symptoms, at the third day of abstinence the patient started to hallucinate and the following day's symptoms were aggravated with increased hallucinations and confusion. After treatment with benzodiazepines the psychosis resolved.
Conclusion: Phenibut withdrawal symptoms can become severe and have similarities to Baclofen, GHB, benzodiazepine and alcohol withdrawal. Benzodiazepines and supportive care seems to be the most effective choice of treatment for objective abstinence symptoms.

Keywords: *Phenibut, withdrawal symptoms, substance-induced psychosis*

Introduction

Phenibut is a drug developed in the Soviet Union in the 1960s. In Russia, it is used clinically to treat anxiety, stuttering in children and alcohol withdrawal symptoms and to improve sleep (Ban et al., 1998; Lapin, 2001). In Europe and the United States, it is marketed as a dietary supplement and legally available without prescription on the Internet. Two previous case reports (Odujebe et al., 2008; Magsalin & Khan, 2010) about withdrawal symptoms have been published, and there are many more on different Internet forums. This is a case report of a young man with a previous history of substance abuse experiencing severe withdrawal symptoms and psychosis after discontinuation of phenibut. As this patient sought medical

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care a few hours after taking the last dose, we had the opportunity to follow him throughout the entire abstinence period.

Case report

The patient is a somatically healthy man in his mid-twenties. He has a history of mixed substance abuse, predominantly benzodiazepines and opiate addiction. However, he has no psychiatric diagnosis except for substance abuse and has not experienced psychotic symptoms previously except after taking hallucinogens. For the last 2 years, he has been in continuous contact with "The Center for Dependency Disorders in Stockholm", where he was first weaned off opiates. This was followed by inpatient care to quit benzodiazepines. Since discharge, he has attended scheduled appointments at the outpatient clinic to prevent relapse. Urine screenings have verified that he has been free from common drugs except for one relapse of benzodiazepines about 2 weeks prior to the present admission. Phenibut cannot be seen in urine screenings. The patient did not take any prescribed drugs other than alimemazin, alimemazine and hydroxyzine to aid sleep. However, after being weaned off benzodiazepines and discharged from hospital the patient searched the Internet to find something that could relieve benzodiazepine cravings and improve social skills. Through Internet discussion forums, he found phenibut in a Swedish web shop selling dietary supplements for athletes and purchased a package of Z-12 that contained phenibut. The recommended dose is up to 1.5 g per day (Lapin, 2001; Magsalin & Khan, 2010), but our patient started with 0.75–1.0 g 6–8 times per day and then increased the dose up to 1.5–2.0 g 8–10 times per day as tolerance developed. This is more than 10 times the recommended dose. He used phenibut for a total of 2 months, and he noted the tolerance development just after 1 week of daily usage. The patient had combined phenibut with alcohol a few times and then experienced a severe hangover. A few days before admission to hospital our patient realized he was going to run out of phenibut and cut down his doses to 15 g per day. He took the last dose in the morning and then contacted his addiction medicine physician who referred him to the inpatient addiction medical clinic (we call this as day 1 of abstinence). Two hours after the last dose of phenibut the patient started to experience subjective withdrawal symptoms. During the first 2 days of abstinence, these symptoms were feelings of unreality, worthlessness, inner worries, downheartedness, light and sound sensitivity, muscle pain, insomnia, anxiety, muscle twitches, heart palpitations and fatigue.

During admission the patient was sober, and urine screening (later verified by blood sample) was negative on all tested substances: amphetamine, methamphetamine, benzodiazepines, cocaine, opiates, tetrahydrocannabinol, morphine alkaloids, Internet drugs, spice, and herbal and mushroom drugs. Given the patient's previous benzodiazepine addiction we wanted to avoid treating him with benzodiazepines. A fortnight before admission the patient had tried to self-medicate with pregabalin and experienced relief from subjective phenibut withdrawal symptoms; however, pregabalin also has the potential of being addictive. Therefore, the patient received gabapentin in an attempt to relieve subjective abstinence symptoms and promethazine and levomepromazine as anxiolytic and sedative medication, respectively.

On the third day of abstinence the patient experienced increased severity of subjective symptoms and also felt changes between hot and cold and changed perception of sound. Objectively he was more stressed, talked quickly and started to have intermittent visual hallucinations where he saw patterns on the walls and people in the room. On the fourth day

of abstinence the patient exhibited intention tremor and began to give long diffuse answers to questions. He had trouble keeping his train of thoughts in a conversation and was anxious and experiencing feelings of very low self-esteem. He still had visual hallucinations when he was alone in his room, but during conversations he was aware that the hallucinations had not been real. The patient received haloperidol with satisfactory results. However, during the fifth and the sixth days of abstinence the symptoms were aggravated; the patient became disoriented and openly psychotic with both visual and auditory hallucinations. The patient first received olanzapine and promethazine, but he slept only a few hours and the symptoms could not be controlled. He then received 30 mg diazepam and additional nitrazepam whereupon he fell asleep. After this, during days 7–11 the patient was orientated and did not experience more hallucinations. He could not remember much of what had happened during the past days. During the entire time at hospital he was circulatory and respiratory stable and never became aggressive. On day 11 he was discharged from hospital with a low-dose oxazepam that was intended to be phased out. He was referred back to outpatient addiction medical care.

Discussion

Phenibut (synonyms: fenibut, phGABA) has anxiolytic, tranquilizing and nootropic (cognition-enhancing) effects. It has been used in Russia to treat several different conditions and was also used by Soviet cosmonauts during the Apollo-Sojuz space flight (Ban et al., 1998). In the United States and in Europe, phenibut is available through Internet purchase. It is marketed as a nutritional supplement to improve sleep. There are about 300 publications concerning phenibut, but the vast majority of these are in Russian and appear to come from the research group that discovered and developed the drug (Ban et al., 1998). In this literature, few side effects have been reported (somnolence in geriatric patients), but tolerance development, as early as after 2 weeks of treatment, has been acknowledged as a drawback of phenibut therapy (Ban et al., 1998).

Our patient's symptoms are similar to those described in the previous two case reports about phenibut withdrawal. Similar to Dr. Magsalin and Dr. Khan's patient, the onset of withdrawal symptoms was 2–4 hours after the last dose of phenibut and our patient also experienced nervousness, inner shakiness, fatigue, poor appetite, heart palpitations, nausea and insomnia and felt tense and keyed up (Magsalin & Khan, 2010). However, our patient was not agitated and did not feel easily annoyed. Similar to Dr. Odjube, Dr. Hoffman and Dr. Nelson's patient who was admitted to hospital on the third day of abstinence, our patient also developed psychosis, hallucinations and insomnia, but not agitation (Odujebe et al., 2008). Given that our patient had repeated drug screenings, all of which were negative, with one exception of benzodiazepines, we believe it is unlikely that his symptoms were caused by ingestion of some drug other than phenibut. It should not be an acute effect of the drug, as symptoms developed through several days of abstinence and the half-life of the drug is 5.3 hours (Lapin, 2001). However, it is questionable if physical withdrawal symptoms could develop after just 2 hours, given this half-life. It is more likely that the early symptoms experienced by our patient were related to anxiety due to discontinuation of the drug.

Phenibut acts as a GABA-mimetic mainly on $GABA_B$ receptors and to some extent on $GABA_A$; it has also been shown to stimulate dopamine receptors (Lapin, 2001). This mechanism is similar to that of baclofen, which is the *p*-Cl derivative of phenibut (Lapin, 2001) and that of gamma-hydroxybutyric acid (GHB) although the mechanism of GHB is not

exclusively on $GABA_B$ receptors (Carter et al., 2009). The withdrawal symptoms of phenibut also appear to have similarities to baclofen, GHB, benzodiazepine and alcohol withdrawal. Baclofen withdrawal has been reported to present on days 2–4 of abstinence or decreased dosage, with confusion, agitation, auditory and visual hallucinations and seizures (Terrence & Fromm, 1981). However, baclofen withdrawal was noted only after many months of therapy. GHB was previously used as a "health product" among bodybuilders to improve sleep, just as phenibut is today. Common symptoms of GHB withdrawal that have been reported are, for example, tremor, tachycardia, anxiety, hallucinations, delusions or paranoia, psychosis in clear consciousness, delirium and insomnia (McDonough et al., 2004). Benzodiazepines and alcohol mainly activate $GABA_A$ receptors contrary to the activation of $GABA_B$ by phenibut. However, symptoms reported in benzodiazepine abstinence are similar, for example, restlessness or agitation, increased anxiety, loss of appetite, hyperacusis, nausea, fatigue, insomnia, tremor, palpitations, muscle aches, photophobia, confusion, psychosis and seizures (Schweizer & Rickels, 1998).

From our own case and from the previously reported cases of phenibut withdrawal we conclude that tolerance and withdrawal symptoms of phenibut can develop rapidly, as early as after only 1 week of daily use. Withdrawal symptoms can become severe with confusion, hallucinations and agitation. The most effective treatment seems to be benzodiazepines and supportive care. Gabapentin or pregabalin might have some effect at least on subjective symptoms, while antipsychotics and serotonergic anxiolytics were not enough to control the symptoms in our patient.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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