Two Cases With Antiepileptic Barbexoclone (Maliasin®) Addiction

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ÖZET

Antiepileptik barbeksaklon (maliasin®) bağımlılığı olan iki olgu

Barbeksaklon (Maliasin®), antiepileptik olarak değerlendirilen ve epilepsi tedavisinde etkinliği kanıtlanmış bir ilaçtır. Bununla beraber, kliniğimize barbeksaklon kötüye kullanımı tanısı ile yatarak tedavi başvurusunda bulunan olguların sayıları da giderek artmaktadır. Bu yazıda, bir bağımlılık merkezinde yatarak tedavi olan ve barbeksaklon bağımlılığı tanısı alan iki olgu sunulmuştur. Ayrıca bu olgular doğrultusunda, reçeteli ilaçların endikasyon dışı kullanımları tartışılmıştır.

Anahtar kelimeler: Antiepileptik, barbeksaklon, bağımlılık, reçeteli ilaç

ABSTRACT

Two cases with antiepileptic barbexoclone (maliasin®) addiction

Barbexoclone (Maliasin®) is an antiepileptic drug, which has been found to be effective in the treatment of epilepsy. Inpatient treatment seeking cases with the diagnosis of barbexoclone abuse accumulate. In this report, we presented 2 inpatient cases in an addiction treatment center with barbexoclone dependence. Also we discussed the non-medical use of prescribed drugs according to these cases.

Key words: Antiepileptic, barbexaclone, dependence, prescribed drug

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INTRODUCTION

The American Food and Drug Administration sees the abuse of drugs that act on the central nervous system (CNS) as a major social problem and is trying to take measures to prevent it (1). Psychotropic drugs or other CNS-related drugs may be abused. For example, tianeptine (2,3), an antidepressant obtainable with a normal prescription and quetiapine (4), an antipsychotic drug, are drugs prescribed for psychiatric treatment but abused. Moreover, there are reports of patients abusing drugs containing such substances as ephedrine/pseudoephedrine (metcatinone) (5), which is not included in routine psychiatric treatment and obtainable with normal prescription, or pheniramine (6), an antihistaminic agent.

Prescribed medicines may be abused for various reasons, including self-treatment or seeking fun and excitement. In a study of those using prescribed medicines non-medically, around 13% were evaluated as the fun-seeking sub-group, 39% as the self-treatment sub-group, and 48% as a mixed sub-group. While the likelihood of substance use or abuse was lower in the self-treatment sub-group, substance abuse was detected in about half of other sub-groups (7).

Barbiturate and benzodiazepines used in the treatment of epilepsy carry a risk of addiction. In the sole study conducted on this issue, it was concluded that barbiturates and benzodiazepines do not pose a significant risk of substance addiction in epilepsy patients (8). In that study, the physiological variables of addiction (tolerance and withdrawal syndrome) were detected in about half of the sample, but psychological variables (craving and loss of control) were detected in less than ten percent of the sample. Forty-five percent of patients developed a tolerance to the drugs' anti-convulsant effect and 48% reported symptoms of physical withdrawal (8).

Barbexoclone (Maliasin®) is a salt compound of phenobarbital and prophylhexedrine. Barbexoclone, reported to be as effective as phenobarbital and better tolerated, was introduced in 1983. One hundred milligrams of barbexoclone is the equivalent of 60 mg phenobarbital. When phenobarbital was first introduced, its potential for addiction created difficulties (9). Abuse of prophylhexedrine (eight percent of the MSS stimulating effect of amphetamines) was reported after the introduction of an inhaler containing

prophylhexedrine in 1949, owing to its vasoconstriction effect, and abuse of this drug continued to be reported in subsequent years, albeit rarely (10).

CASES

This article presents two inpatient cases diagnosed with barbexoclone addiction at the Substance Rehabilitation Department of the Alcohol and Substance Research, Treatment and Training Center (AMATEM) in Bakırköy Prof. Dr. Mazhar Osman Research and Training Hospital for Psychiatry, Neurology and Neurosurgery. The article discusses the non-indicated use of prescription drugs in these cases. During their hospitalization in the department, the patients were given the Michigan Alcoholism Screening Test (11,12), Beck Depression Inventory (13,14), and State Continuous Anxiety Inventory (15) tests, which have been subjected to Turkish validity and reliability studies. The features of the patients according to common scales and evaluations are shown in Table 1.

CASE 1

Y.D. was a 28-year-old single male patient. He was working in the natural gas business with his father until the last month and a half before he was taken to AMATEM. Based on a request submitted by his family, the patient was brought to the AMATEM polyclinic with a letter from his district governor's office indicating that "he is a substance abuser and occasionally disturbs people around him". He was accompanied by the police and ambulance and hospitalized with the pre-diagnosis of barbexoclone abuse in July 2009. The patient stated that he had last used around ten tablets of barbexoclone three weeks before his admission to our clinic.

The patient served two and a half years in prison for insubordination during his military service in 2005. The physician in the prison started the patient on barbexoclone as a muscle relaxant during this period. Over the next four years, the patient continued to use barbexoclone (25 mg) once or twice a week, 10 tb/day. He described the effect of the substance as follows: "I think it is relaxing, it reduces my anger when I argue with other people." The patient had first sought admission to AMATEM in July 2008 and said that he lost his temper quickly and he used barbexoclone to reduce his anger and to avoid occasional feelings of emptiness inside. When the patient was hospitalized in AMATEM in 2009, he reported that he had been smoking for three years and rarely drank alcohol. Six months before he was brought to our unit, he had attempted to be treated and stayed for two days in another hospital for the same reason.

The patient's family history includes cocaine use by his sister and alcohol and clonazepam (Rivotril®) abuse by his cousin. Both of his relatives had been admitted to AMATEM for treatment.

No significant symptoms were detected in the patient's psychiatric examination. The neurological examination and routine laboratory test were within normal limits. His treatment was set as diazepam 40 mg/day, mirtazapine 15 mg/day, and risperidone 1 mg/day. No withdrawal symptoms were observed during follow-up care and the diazepam dose was reduced and then stopped. The patient was discharged on the tenth day of hospitalization at his own request; he gave excuse of having to work. The patient did not come for his polyclinic check-ups and was not reachable by phone.

CASE 2

Y.D. was a 26-year-old single male patient. He was a senior at the Faculty of Open University, School of Management. He lived with his parents and one brother. The patient requested admission to the AMATEM polyclinic wanting to give up barbexoclone and was admitted to the department in December 2009. The patient said that he had returned from military service six months ago and started to use barbexoclone to relax since he could not get used to the civilian environment, had psychological problems, and frequently quarrelled with his girlfriend. He learned about the drug's relaxing effect from a friend. The patient had used five to ten tablets of barbexoclone in the beginning, but had recently upped the dose to 40

Table 1: Results of patients according to scales and assessments

Scales and Evaluations	Case 1	Case 2	Cut-off Point of Scale
Michigan Alcoholism Screening Test	12	28	5/9
Beck Depression Inventory	22	15	17
State Continuous Anxiety Inventory-State	29	27	44
State Continuous Anxiety Inventory-Continuous	42	41	44
Defining self as addicted	+	+	
Tolerance	+	+	
Deprivation	Defined, not observed	-	
Loss of control	+	+	
Craving	+	-	

to 50 tablets. One day before he requested admission from our polyclinic, he took 30 tablets of barbexoclone (100 mg). He described the effect of the substance as follows: "It relaxes me, makes me forget my troubles, energizes me, and cheers me up easily.

Two months before he was admitted to our unit, the patient had been treated as an inpatient, for the same reason, in another hospital for 15 days. He had not used barbexoclone for about a month and a half, but started again on a day when he had problems with his girlfriend and was very depressed.

Stating that he had gone through a difficult period in the year that he took the university entrance exam, since he broke up with his girlfriend of four years, the patient chose not to go to university that year. During that period, he smoked marijuana under pressure from his friends to "relieve his pain" and the continued using it for another six months. Subsequently, he gave up marijuana without getting any treatment assistance. He tried ecstasy a few times, but did not continue. The patient also reported that he had smoked for 15 years and rarely drank alcohol. He did not describe any history of alcohol or substance abuse in his family or close relatives.

There was no significant symptom in his psychiatric examination. There was nystagmus to the sides, disartric speech, difficulty in the finger – nose test (more on the left), dysdiadochokinesia, and ataxic gait. The neurological consultation attributed the patient's symptoms to barbexoclone intoxication. Laboratory tests were within normal limits.

The patient was started on diazepam 10 mg/day, considering the risk of epileptic seizure and phenobarbital withdrawal symptoms. Phenobarbiturate withdrawal symptoms were not observed. On the third day after Maliasin® was discontinued, the patient started follow-up care without drugs. Completing the detoxification program and with a normal neurological examination result on day 21 of his treatment, the patient was discharged to attend the outpatient therapy program.

DISCUSSION

Substance dependence is defined as "using the substance in a higher dose than recommended doses, unsuccessful attempts to stop use, presence of withdrawal symptoms and development of tolerance" in DSM-IV-TR (16). Our cases meet the substance dependence diagnosis criteria of DSM-IV with development of tolerance, use of high doses, previous unsuccessful attempts at cessation through inpatient treatment and with symptoms of loss of control. The presence of cittosis and need for hospital admission also support this diagnosis. Moreover, the sedative and stimulating effect of the drug can be cited as a reason of the inability to reduce the amount used.

The potential for abuse of prescribed medicines is known and the practice of red and green prescription(specific prescriptions controlled by ministry of health) was started to prevent this situation. Meperidine (17) and benzodiazepines (18) are examples of drugs that fall under the red or green prescription system. Prescription drugs used for non-medical reasons include analgesics containing sedatives, hypnotics, anxiolytics, opioids, or caffeine (19).

It is important to be able to determine in whom abuse of prescribed medicines may develop. Individuals

with a history of substance abuse are known to be inclined to abuse drugs, particularly drugs that act on the central nervous system. Yet little is known about the risk status of individuals with no substance abuse in their history (20). For example, quetiapine (20) abuse is predominantly observed in those with a history of substance use disorder, while ephedrine abuse was reported in a patient with no history of other substance abuse history (5). Tianeptine abuse was seen both in a case with a diagnosis of substance use disorder in his history (2) and in a case with no diagnosis of substance use disorder in his history (3). There was substance use in the family history of the first case mentioned and in the personal history of the other case. This indicates that evaluation of not only personal history, but family history may also be important in determining the risk of barbexoclone abuse.

Many anti-convulsant drugs such as phenobarbital (21), carbamazepine, lamotrigine, topiramate, gabapentin or valproic acid are used in the treatment of alcohol/substance dependence (22). Substance abusers are likely to abuse drugs that relax them, such as quetiapine (4). The patients described themselves as addicted and over time developed a tolerance to the effects of the drug. Moreover, loss of control and craving, psychological variables of addiction, were detected in both cases. However, no withdrawal symptoms were observed during the follow-up of these patients. This may be due to the immediate start of benzodiazepine treatment because of the risk of seizure.

The motivation giving rise to non-medical indication use of barbexoclone is believed to stem from its sedative or anxiolytic (tranquilizing) effect, rather than from a desire to "get high". If taken in high doses, with alcohol or other sedative drugs, this effect may be even stronger. Phenobarbital sedation is a common side effect. In barbexoclone, an anticonvulsant preparate, the aim is to connect to phenobarbital, the levo isomer of prophylhexedrine, and eliminate the sedative effect (10). Prophylhexedrine is an CNS stimulant rarely preferred among stimulant abusers. Only the second patient mentioned noted "energizing" and "cheering" effects, in addition to the drug's "relaxing" effect, among his motivations for using the drug.

With regard to depressive symptoms, the first case passed the break point, while the second case scored close to the break point. A similar result applies to both cases for continuous anxiety levels. It is reported that epileptic patients do not develop an addiction to anti-epileptics because their expectations regarding the drug are related to its anticonvulsant effect, rather than its psychotropic effect (8). Both patients may have started to use barbexoclone in order to deal with their life problems or relax their minds – in other words, in an attempt to self-medicate – and may have subsequently continued to use it (23). It is apparent, however, that the patients experienced not only family, occupational, and social problems, but also health problems due to their drug use. These problems intensify the person's negative feelings and in turn he or she uses the substance again to relieve these feelings. This situation leads to a vicious cycle over time.

One must not forget, therefore, that drugs acting on the central nervous system (CNS) obtainable with a normal prescription can be abused by the patient. Barbexoclone is an antiepileptic and a drug that acts on the CNS, and may be abused. We consider it important to question a patient's personal or family history of substance abuse and evaluate the negative effect such as anxiety or depression when prescribing drugs of this type. If any of these risks is present, physicians must consider different treatment alternatives or closely monitor the patient's drug use habits.

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