The Abuse Potential of Carbamazepine: A Case Report

Karbamazepinin Olası Kötüye Kullanımı: Olgu Sunumu

Leman İnanç[1], Merih Altıntaş[2], Ece Yazla[3]

ABSTRACT

Carbamazepine is used for reduction of aggression associated with psychiatric disorders. Carbamazepine is not widely known or recognized as a drug with abuse or misuse potential. In our literature search we have encountered only one case report about the abuse potential of carbamazepine. Here we report a case of carbamazepine misuse we encountered in Turkey. We speculate that the patient's usage seems to have started with misuse and proceeded into abuse of the medicine. This case study points at a possibility of misuse and perhaps even a risk of abuse of Carbamazepine..

Key Words: Carbamazepine, abuse, addiction.

ÖZET

Karbamazepin psikiyatrik bozukluklardaki agresyonun azaltılmasında kullanılmaktadır. Karbamazepin reçete önerisi dışında kullanımı veya kötüye kullanım potansiyeli olan bir ilaç olarak bilinmemektedir. Geçmiş literatürde karbamazepinin kötüye kullanım potansiyelinden bahseden sadece bir olguya rastladık. Bu yazıda, Türkiye'de karbamazepin kötüye kullanımı olan bir olgu sunulmaktadır. Bu ilacın, önerilen dozun dışına çıkmakla başlayıp kötüye kullanım şeklinde devam edildiği düşünülmektedir. Bu olgu, karbamezapinin reçete önerisi dışında kullanma eğilimi veya kötüye kullanım riski olduğunu göstermektedir.

Anahtar Kelimeler: Karbamazepin, kötüye kullanım, bağımlılık.

INTRODUCTION

Medications are effective when they are used properly but some of them can be addictive and those are often abused or misused. Mood stabilizers have been established as a safe and effective treatment in coexisting substance abuse (1). Mood stabilizers especially carbamazepine and lithium are significantly effective for reduction of aggression associated with some psychiatric disorders (2).

Carbamazepine received FDA (Food and Drug Administration) approval for the treatment of psychomotor and grand mal seizures and trigeminal neuralgia and was also approved for manic and mixed episodes of Bipolar I disorder (3).

Carbamazepine is not recognized as a drug with abuse potential and data on carbamazepine misuse and addiction are lacking in the previous literature. We have encountered only one case report about the abuse potential of carbamazepine where it was used solely in order to get the feeling of euphoria (4).

Here, we also report a case about the potential abuse of carbamazepine for euphoria. To our knowledge, this is the first case report of carbamazepine misuse and abuse in Turkey.

[1] Yrd. Doç. Dr., Muğla Sıtkı Koçman Üniversitesi, Ruh Sağlığı ve Hastalıkları
[2] Uzm. Dr., Erenköy Ruh ve Sinir Hastalıkları E.A.H.
[3] Yrd. Doç. Dr., Hitit Üniversitesi

Not: 15-19 Nisan 2015 tarihlerinde Antalya'da yapılan 7. Psikofarmakoloji Kongresinde poster özeti olarak sunulmuştur. Aynı zamanda poster özeti olarak Klinik Psikofarmakoloji Bülteninde 2015; 25 (Ek1): S:210'da yayınlanmıştır.

Address reprint requests to:
Leman İnanç, Muğla Sıtkı Koçman Üniversitesi, 48000 Kötekli, Muğla - TURKEY

E-mail address:
leman.inanc@gmail.com

Phone:
+90 (356) 215 00 70

Date of submission:
October 28, 2016

Date of acceptance:
November 30, 2016

CASE REPORT

The patient is a 28 years-old, single and primary school graduate man. He is living with his mother and working irregularly. He has a previous psychiatric history of psychosis. His psychotic disorder appeared six years ago because of substance abuse. The first episode was characterized by irritability, agitation, aggressive behavior, delusions, decreased sleep and psychosocial dysfunction. For the treatment of those psychotic symptoms, he was prescribed zuclopenthixol depot and quetiapine. This treatment produced a good effect on his psychotic thought content, irritability and decreased sleep. Three years ago he was presented to mental health service for the second time with agitation, irritability, aggressive behavior and somatic delusions and diagnosed with substance induced psychotic disorder. The patient was treated by quetiapine. The dosage was adjusted and a mood stabilizer carbamazepine was added to the treatment. He received carbamazepine for several weeks with quetiapine. Carbamazepine was maintained at 400 mg/day for several weeks. As a result, his behavioral problems improved.

His relatives brought him to hospital due to taking high dose of carbamazepine and uncontrollable behavior. On presentation to the emergency department, he reported that he had taken his last dose of carbamazepine some hours before. He complained of abdominal pain, nausea, several episodes of vomiting and having trouble sleeping. At the emergency department his carbamazepine blood level was measured to be at 15,4 µg/ml (4-12 µg/ml). He was closely monitored for vital signs, cardiac rhythm and his carbamazepine serum levels were followed. No pathological signs were found in his physical examination. He had no comorbid medical illness and his family history was also unremarkable. There were no neurological signs or symptoms like ataxia, nystagmus, mydriasis, movement disorders and no anticholinergic signs. The patient's examination did not suggest any neurological symptoms so that during his monitoring in emergency room no neurological imaging was requested. Biological tests including routine blood count and urine examination were normal with exception of the increase in mean corpuscular volume. The possibility of megaloblastic anemia was considered. He was started on an oral B12 supplementation. He had hyponatremia with sodium levels of 127 mEq/L (136-145 mEq/L). Hyponatremia was asymptomatic.

Two days after he was discharged from the emergency department, he was admitted to our ward presenting irritability and agitation symptoms. His carbamazepine level was down to 1 µg/ml (therapetical reference range being 4-12 µg/ml), with sodium level at 144 mEq/L (136-145 mEq/L). Two weeks after starting the patient on risperidone and quetiapine, a successful improvement was observed with reduction of agitation and aggressive behaviour.

He had stopped abusing substance 3 years ago and had been taking high doses carbamazepine for three years. He admitted to going to drugstores and buying boxes of drug containing 400 mg of carbamazepine. The patient admitted to consuming approximately 10 pills (equivalent to 4000 mg) of carbamazepine daily. He reported that a psychiatrist had prescribed carbamazepine three years ago to relieve his aggressive behavior and due to anticraving efficacy. Initially carbamazepine provided relief for both conditions. Then he started taking excessive amounts of carbamazepine one or two times a week for its euphoric effects. Gradually he increased the dose of carbamazepine to 3200-4000 mg daily. He reported that he had felt euphoric while on high doses of carbamazepine and that afterwards he had a little dizziness and nausea. On experiencing nausea he would cut down the carbamazepine intake. The euphoric effects and relief reportedly lasted for six hours. After the pass of the euphoria the patient reported to overdose again thus overdosing twice daily. He failed to cut down the drug usage and his drug cessation attempts did not last for more than three days.

DISCUSSION

Medicine abuse is common in many countries but drugs that are abused vary according to the location. Often these drugs are codeine based medicines, cough products, sedative antihistamines, decongestants and laxatives (5). Drug misuse is characterized by using a drug out

of intended purposes, taking it in higher amount, for a longer period than prescribed and taking it out of health care professionals' control (6, 7).

Our patient was prescribed carbamazepine and he was taking it in higher than prescribed doses. This type of use is compatible with the concept of misuse. The patient reported a euphoric feeling when taking the drug at doses higher than prescribed. He used the drug in order to ''get high'' so this complies with the term abuse. He tried but could not cease using the drug; he had cravings for the drug as well. He made several attempts to decrease his use of carbamazepine, but afterwards felt very anxious and hostile towards his family members. In the initial period of usage, the patient started using carbamazepine in order to get a relief but later the patient continued using it for its euphoric effect. Although misuse and abuse are frequently used interchangeably, his usage seems to start with misuse and proceed to abuse of the drug (6).

Carbamazepine is an anticonvulsant possessing GABAergic activity and NMDA blockage (8). This may be responsible for anxiolytic effect of the drug and may contribute to the abuse of the drug (9, 10). Hosseini et al suggested that being the only anticonvulsant with tricyclic structure may be a possible mechanism of the euphoric effect (4). The euphoric effect of alcohol and carbamazepine taken together has been referred to in the literature (11). Our patient however did not have a history of alcohol abuse or any other drug abuse or addiction for the last three years. We know of only one other case of a patient diagnosed with a bipolar disorder that has been reported for using carbamazepine solely for its euphoric effect (4).

Normal reference range of carbamazepine is 4 to 12 µg/ml. In neurological examination in case of toxicity, the expected pathological findings are nystagmus, dysarthria, diplopia and ataxic walking (12). Our patient complained of abdominal pain, nausea, vomiting and epigastric pain but had no other neurological signs at a level of 15 µg/ml (4-12 µg/ml). He reported to stopping taking medicine when these abdominal symptoms occur. In our case the patients' tolerability seems to be over the reference range. This condition may be due to CYP450 enzyme polymorphism. CYP450 enzyme polymorphism can cause unexpected drug response, unanticipated adverse reactions and can cause drug toxicities (13, 14). We postulate that when a high serum carbamazepine level is encountered without usual symptoms of overdose the possibility of abuse should be evaluated.

Carbamazepine induces CYP3A4 and other oxidative enzyme systems in the liver and accelerates metabolism of other drugs that are used simultaneously. Inhibition of its liver metabolism by other drugs can cause toxic serum concentrations of carbamazepine (15). Patients should be warned about possible adverse effects of other drugs while on carbamazepine. Hence there is also risk of accidental carbamazepine overdose when another drug inhibits the liver metabolism even though the patient is not actually taking high doses of carbamazepine.

Carbamazepine is generally accepted as a non-addictive drug. This case study warns us that carbamazepine may actually have an abuse potential.

REFERENCES

1- Maremmani I, Pacini M, Lamanna F, et al. Mood stabilizers in the treatment of substance use disorders. CNS Spectr 2010; 15: 95-109.
2- Jones RM, Arlidge J, Gillham R, et al. Efficacy of mood stabilisers in the treatment of impulsive or repetitive aggression: systematic review and meta-analysis. Br J Psychiatry 2011; 198: 93-98.
3- Post RM, Ketter TA, Uhde T, Ballenger JC. Thirty years of clinical experience with carbamazepine in the treatment of bipolar illness: principles and practice. CNS Drugs 2007; 21: 47-71.
4- Hosseini SH, Ahmadi A. Abuse of CBZ for euphoria. Drug Res 2014; 64: 1-2.
5- Cooper RJ. Over-the-counter medicine abuse: a review of the literature. Journal of Substance Use 2013; 18: 82-107.
6- Wazaify M, Shields E, Hughes CM, McElnay JC. Societal perspectives on over-the-counter (OTC) medicines. Family Practice 2005; 22: 170-176.
7- Hughes GF, McElnay JC, Hughes CM, McKenna P. Abuse/misuse of non-prescription drugs. Pharm World Sci 1999; 21: 251-255.
8- Barrons R, Roberts N. The role of carbamazepine and oxcabazepine in alcohol withdrawal syn-

drome. J Clin Pharm Ther 2009; 35: 153-167.
9- Ketter TA, Post RM, Theodore WH. Positive and negative psychiatric effects of antiepileptic drugs in patients with seizure disorders. Neurology 1999; 53 (Suppl.2): 53-67.
10- Aydın PC, Akyalcin S, Mete L. Antiepileptic drugs in the treatment of anxiety disorders. Current Approaches in Psychiatry 2009; 1: 80-94.
11- Sullivan G, Davis S. Is carbamazepine a potential drug of abuse? J Psychopharmacol 1997; 11: 93-94.
12- Soderstrom J, Murray L, Little M, Daly FFS. Toxicology case of the month: carbamazepine overdose. Emergency Medicine Journal : EMJ 2006; 23: 869-871.
13- Ogu CC, Maxa JL. Drug interactions due to cytochrome P450. BUMC Proceedings 2000; 13: 421-423.
14- Lynch T, Price A. The effect of cytochrome P450 metabolism on drug response, interactions, and adverse effects. Am Fam Physician 2007; 76: 391-396.
15- Spina E, Pisani F, Perucca E. Clinically significant pharmacokinetic drug interactions with carbamazepine. An update. Clin Pharmacokinet 1996; 31: 198-214.