

A Case with Status Epilepticus and Cardiac Arrest After Bupropion Overdose

Ferda Ilgen Uslu¹,
Nazan Simsek Erdem¹,
Selahattin Yagan¹

¹Neurologist, Antalya Ataturk State Hospital,
Antalya - Turkey

ABSTRACT

A case with status epilepticus and cardiac arrest after bupropion overdose

Bupropion is an atypical antidepressant used for the treatment of severe depression and smoking cessation. Hallucinations, agitation, and seizures are the commonest central nervous system effects after a bupropion overdose. Cardiac manifestations are uncommon. We present a 19-year-old female who presented to the emergency department with asymmetric tonic seizures and then went into cardiac arrest. She was intubated and mechanically ventilated and then admitted to intensive care unit. Brain computerized tomography and magnetic resonance imaging scans were normal at admission. Clinical features resolved completely with symptomatic treatment. She had no previous history of epilepsy, head trauma, infection, family history, and no risk factors for developing epilepsy. There was no history of alcohol abuse, suicide attempt, or depression. She only was a heavy smoker. When she completely regained consciousness, she said to have ingested 15 tablets of bupropion XL (4.5g), which belonged to her mother, with the intention of suicide. Overdose of bupropion may become more common with increasing therapeutic use and may cause life-threatening conditions. Patients receiving high doses of bupropion should be closely monitored cardiologically and neurologically. Patients should receive cardiac monitoring until the accompanying tachycardia has abated and any QRS or QTc interval prolongation has been excluded.

Keywords: Bupropion overdose, cardiac arrest, seizures

ÖZET

Aşırı doz bupropion alımı sonrası status epileptikus ve kardiyak arrest olan bir olgu sunumu

Bupropion ciddi depresyon ve sigara bıraktırma tedavisinde kullanılan atipik bir antidepressandır. Halüsinasyonlar, ajitasyon ve nöbetler aşırı doz bupropion kullanıma bağlı görülen en yaygın santral sinir sistemi yan etkileridir. Kardiyak bulgular nadirdir. Bu makalede acile asimetric tonik nöbetler nedeniyle başvuran ve ardından kardiyak arrest gelişen 19 yaşında kadın hasta sunduk. Hasta entübe edildi, mekanik ventilatöre bağlandı ve yoğun bakım ünitesine alındı. Beyin tomografisi ve manyetik rezonans görüntüleme incelemeleri normaldi. Semptomatik tedavi ile sekelsiz iyileşti. Daha önce epilepsi, kafa travması, enfeksiyon, ailesinde hastalık ya da epilepsi gelişmesine neden olabilecek diğer risk faktörleri yoktu. Alkol kullanımı, intihar girişimi ve depresyon öyküsü yoktu. Yoğun sigara kullanımı mevcuttu. Hasta tamamen kendine geldiğinde intihar girişimi için annesine ait olan 15 tablet (4.5gr) bupropion XL aldığını ve ifade etti. Bupropion'un tedavi amaçlı kullanımın artması ile aşırı doz kullanımı yaygınlaşmakta ve yaşam tehdit edici bir durum oluşturmaktadır. Yüksek doz bupropion kullanan hastalar kardiyak ve nörolojik açıdan yakından takip edilmelidirler. QRS veya QTc aralığında uzama bulunanlarda kullanımdan kaçınılmalı, taşikardisi olan hastalar ise taşikardi düzeleneye kadar yakın gözlem altında tutulmalıdır.

Anahtar kelimeler: Aşırı doz bupropion kullanımı, kardiyak arrest, nöbet



Address reprint requests to / Yazışma adresi:
Neurologist Ferda Ilgen Uslu,
Antalya Ataturk State Hospital, Gulluk Caddesi,
07040 Muratpasa/Antalya, Turkey

Phone / Telefon: +90-432-2177607/219

E-mail address / Elektronik posta adresi:
ferdailgen@yahoo.com

Date of receipt / Geliş tarihi:
April 16, 2014 / 16 Nisan 2014

Date of acceptance / Kabul tarihi:
November 9, 2014 / 9 Kasım 2014

INTRODUCTION

Bupropion is an atypical antidepressant marketed for the treatment of severe depression, anxiety disorders accompanying alcoholism and bipolar

disorder; and, more recently, smoking cessation (1). Hallucinations, agitation, and seizures are the most common central nervous system effects after a bupropion overdose (2,3). Seizures occur both in therapeutic doses and following overdose of bupropion.

The mainstay of treatment for bupropion overdose is supportive care (1). Cardiac manifestations are uncommon (except for tachycardia); nevertheless, overdose with more than 1.5g has been associated with disturbance of intraventricular conduction and prolongation of the QT interval (4).

Here we present a 19-year-old female who ingested 4.5g bupropion, developed asymmetric tonic seizures and went into cardiac arrest. The patient was resuscitated and followed in the intensive care unit (ICU); clinical features resolved completely with symptomatic treatment.

CASE

A 19-year-old previously healthy female was found unresponsive at home by her mother. She had seizures in the ambulance and the emergency room, characterized by tonic-clonic seizure, and loss of consciousness. She was given diazepam and then phenytoin intravenously for status epilepticus. Complete blood count and serum chemistries were normal. Electrocardiogram showed sinus tachycardia (heart rate was 140 beats per minute) and QTc within normal limit. On the ward, she was confused, her pupils mid-dilated, unresponsive to light, she had ballistic movements, especially in the right arm. After a seizure-free period, she had brief asymmetric tonic seizures, and at the end of third seizure, she went into cardiac arrest. Immediately resuscitated, the patient was intubated and admitted to the ICU, where she was sedated with propofol. Her seizure activity then quickly stopped. Twenty-four hours later, the patient was taken off sedation. She was not having seizures; neurologic examination was normal. She had no previous history of epilepsy, head trauma, infection, family history, and no risk factors for developing epilepsy. There was no history of alcohol abuse. She only was a heavy smoker. According to her mother, she was not known to be taking any drugs and had not previously taken an intentional overdose or expressed any suicidal thoughts. Her MRI and electroencephalography were normal. When she recovered completely, she said that she had ingested

15-20 tablets of a drug for suicide. Her mother found an empty 'bupropion XL 300mg' box in her room. Once she was medically stable, the patient was transferred to the psychiatric unit.

DISCUSSION

Originally approved for the treatment of depression in 1985, bupropion was removed from the International Pharmacopeia one year later because of a significant risk of seizures, mainly identified in sub-populations with epilepsy or a history of head trauma (4). The product was reintroduced in 1989 with special attention being paid to side effects in patients with known epilepsy or suffering from eating disorders (4,5). Bupropion is a selective inhibitor of dopamine and norepinephrine, reuptake. It also possesses anticholinergic activity (6). Bupropion is extensively metabolized by the liver ($t_{1/2}$ approximately 21 hours). Hydroxybupropion, the primary active metabolite is formed by cytochrome P450 [CYP] 2B6 (7). Some drug therapies can also be affected pharmacodynamically by nicotine. However, bupropion does not appear to be affected by cigarette smoking (8). Its mechanism of action in smoking cessation remains unknown. It is well absorbed in the gastrointestinal system and is metabolized in the liver. The half-life of bupropion is 12 hours; it is excreted in the urine (6).

Symptoms of bupropion overdose may include difficulty of breathing or swallowing, dizziness, fainting, shakiness, sweating, confusion, blurred vision, seizure, hallucinations, loss of consciousness, rapid or pounding heartbeat, blurred vision, light-headedness, confusion, lack of energy, and jitteriness (3). Hallucinations, agitation, and seizures are the most common central nervous system effects after an overdose, but physical signs of anticholinergic intoxication such as mydriasis and hyperreflexia are rarely present (2). These side effects might be prolonged with sustained-release forms of bupropion. Our patient was found unconscious in bed, and later she developed seizures and tachycardia and finally went into cardiac arrest. At the same time, she had mydriatic pupils, suggesting intoxication.

Bupropion has a narrow therapeutic margin (3). Seizures occur in both therapeutic doses and with an overdose of bupropion. The risk of seizures associated with therapeutic use of the sustained-release (SR) formulation is 0.1% with doses of no more than 300mg per day (9). The risk for seizures is highly dose-dependent; seizure activity occurred in 21.0% of patients with overdose (3).

Data regarding the risk of seizure with bupropion extended release (XL) is sparse (10). Some studies have suggested that SR and XL bupropion may result in a delayed onset of seizures within 24 hours after ingestion (3). Our patient had ingested the XL form of bupropion, but her seizures had started on the same day.

Cardiac manifestations are uncommon (except for tachycardia); nevertheless, overdose with more than 1.5g has been associated with disturbance of intraventricular conduction and prolongation of the QT interval. With a massive overdose (10g or more), cardiac failure and death can occur in the absence of rapid treatment (9). Our patient had tachycardia without QT

abnormality at first, but then, after seizures, she suffered a cardiac arrest. Her cardiac activity was normal in echocardiography.

Treatment of an overdose of bupropion is supportive, as there is no antidote available. Gastric lavage and oral activated charcoal may be considered within an hour of overdose, but the value of further doses of charcoal or whole bowel irrigation in bupropion overdose has not been established (10). Symptomatic treatment of our patient was successful and led to a full recovery.

In conclusion, overdosing on bupropion may become more common with increasing therapeutic use and may lead to life-threatening conditions. Emergency departments need to be aware of its adverse effects even in therapeutic doses (2,11). Patients receiving high doses of bupropion should be closely monitored cardiologically and neurologically. Patients should receive cardiac monitoring until the accompanying tachycardia has abated and any QRS or QTc interval prolongation has been excluded (2).

REFERENCES

- Morazin F, Lumbroso A, Harry P, Blaise M, Turcant A, Montravers P, Gauzit R. Cardiogenic shock and status epilepticus after massive bupropion overdose. *Clin Toxicol (Phila)* 2007; 45:794-797. [\[CrossRef\]](#)
- Jepsen F, Matthews J, Andrews FJ. Sustained release bupropion overdose: an important cause of prolonged symptoms after an overdose. *Emerg Med J* 2003; 20:560-561. [\[CrossRef\]](#)
- Wilson B, Paul P, Mehta S, Coffey BJ. Hypokalemia secondary to bupropion sustained release overdose. *J Child Adolesc Psychopharmacol* 2013; 23:57-60. [\[CrossRef\]](#)
- Mercerolle M, Denooz R, Lachâtre G, Charlier C. A fatal case of bupropion (Zyban) overdose. *J Anal Toxicol* 2008; 32:192-196. [\[CrossRef\]](#)
- Shepherd G, Velez LI, Keyes DC. Intentional bupropion overdoses. *J Emerg Med* 2004; 27:147-151. [\[CrossRef\]](#)
- Spiller HA, Schaeffer SE. Multiple seizures after bupropion overdose in a small child. *Pediatr Emerg Care* 2008; 24:474-475. [\[CrossRef\]](#)
- Jefferson JW, Pradko JF, Muir KT. Bupropion for major depressive disorder: Pharmacokinetic and formulation considerations. *Clin Ther* 2005; 27:1685-1695. [\[CrossRef\]](#)
- Desai HD, Seabolt J, Jann MW. Smoking in patients receiving psychotropic medications: a pharmacokinetic perspective. *CNS Drugs* 2001; 15:469-494. [\[CrossRef\]](#)
- Balit CR, Lynch CN, Isbister GK. Bupropion poisoning: a case series. *Med J Aust* 2003; 178:61-63.
- Boora K, Cummings MR, Marshall DR. Generalized seizure in three adolescents with bupropion overdose. *J Child Adolesc Psychopharmacol* 2010; 20:159-160. [\[CrossRef\]](#)
- Bhattacharjee C, Smith M, Todd F, Gillespie M. Bupropion overdose: a potential problem with the new 'miracle' anti-smoking drug. *Int J Clin Pract* 2001; 55:221-222.