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Case Report

Delayed status epilepticus due to bupropion and lamotrigine overdose

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Abstract. Bupropion is a well known atypical antidepressant marketed in the United States under the trade name Wellbutrin. In its sustained release form, it is also used for smoking cessation. It lowers seizure threshold and its potential to cause seizures has been widely publicized. Lamotrigine is a broad spectrum anticonvulsant with an extremely favorable side-effect profile and has thus rapidly become the preferred drug for a broad range of seizure types such as absence seizures, primary generalized epilepsy syndromes such as idiopathic generalized tonic-clonic seizures, juvenile myoclonic epilepsy as well as partial (focal) epilepsy. It is also used by psychiatrists as a mood stabilizer. We report a patient who presented with delayed status epilepticus following a failed suicidal attempt after overdosing on bupropion XL and lamotrigine.

Key words: Bupropion overdose, lamotrigine overdose, suicide, status epilepticus

1. Introduction

Bupropion's potential to cause seizures is well described in the medical literature. Lamotrigine is a broad spectrum anticonvulsant drug which also has mood stabilizing property. Overdose of bupropion and lamotrigine can precipitate cardiovascular collapse. A close clinical watch should also be maintained for delayed onset of status epilepticus.

2. Case report

A-71-year old woman with history of cancer, essential hypertension, depression and at least 2 suicidal attempts in the past presented to the emergency room (ER) via emergency medical services (EMS) with altered mental status after intentional bupropion XL and lamotrigine overdose. Patient was last seen normal by family in the afternoon of admission. Around noon she went into another room and later her boyfriend found her on the floor with empty bupropion XL and lamotrigine bottles by her side. Recent stressors included death of 2 family members and prolonged hospitalization of a close friend. On arrival in the ER, she was unresponsive to voice, agitated but moved all limbs spontaneously. The number of tablets ingested and the exact time of ingestion could not be determined with certainty. Electrolytes, hepatic and renal function tests were normal. Patient was admitted to medicine step-down unit to closely monitor cardiovascular and hemodynamic status. Continuous EEG monitoring was initiated to rule out subclinical electrographic seizures as the cause of her altered mental status. Initial EEG showed a diffusely slow theta frequency background with superimposed faster frequencies. About 10 hours later, she went into status epilepticus and had 8 electroclinical convulsions characterized by abrupt onset of rhythmic theta frequency waveforms in the left and right temporal area with rapid generalization (Figure 1). Clinically she was noted to have her head turned to the left. Rapid eye blinking and facial twitching were noted followed by tonic posturing and low amplitude clonic jerks. Interictally she remained disoriented and agitated. Lorazepam 4 mg was given and she was shifted to the intensive care

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unit for close monitoring of her cardiorespiratory status. Her neurological status gradually returned to baseline over the next 36 hours as she fully metabolized the medications she had overdosed on.

Table. Anticonvulsants and antidepressants which have been associated with status epilepticus

Antiepileptic and antidepressant drugs that cause status epilepticus
Antiepileptic drugs
1. Lamotrigine
2. Levetiracetam
3. Carbamazepine
4. Valproic acid
5. Vigabatrin
6. Pregabalin
7. Topiramate
8. Gabapentin
9. Tiagabine
Antidepressant drugs
1. Bupropion
2. Amoxapine
3. Clomipramine
4. Fluoxetine
5. Amitriptyline
6. Citalopram
7. Fluvoxamine

Source: Tan RY, Neligan A, Shorvon SD. The uncommon causes of status epilepticus: a systematic review. Epilepsy Res 2010; 91: 111-122.

2. Discussion

Our patient ingested an unknown quantity of bupropion XL and lamotrigine tablets. We were unable to determine the blood concentration of bupropion as the sample was not drawn in the correct bottle. Lamotrigine level was 12.5 micrograms/mL (therapeutic range 4.0-18.0 micrograms/mL) when measured about 12 hours after presentation to our ER. It is tempting to postulate that over ingestion of bupropion XL was the cause of status epilepticus in our patient as lamotrigine level was in the therapeutic range, but it was only measured 12 hours after presentation to the ER. So it is debatable which drug was responsible for status epilepticus in our case.

Lamotrigine exerts its anticonvulsant effect by acting on presynaptic voltage-gated sodium channels to decrease glutamate release. It is a broad spectrum anticonvulsant and action on voltage activated calcium channels has also been postulated. Its pharmacokinetics follows first-order kinetics with a half life of about 13.5 hours. It does not prolong QT/QTc in healthy subjects though prolongation of QRS interval on electrocardiogram and complete heart block has been reported in patients following lamotrigine overdose (4 grams) (1). Herold reported widening of the QRS interval and right-axis deviation on ECG due to lamotrigine in a patient with known seizure disorder akin to the cardiac effects of other sodium channel blockers such as tricyclic antidepressants (TCAs) (2).

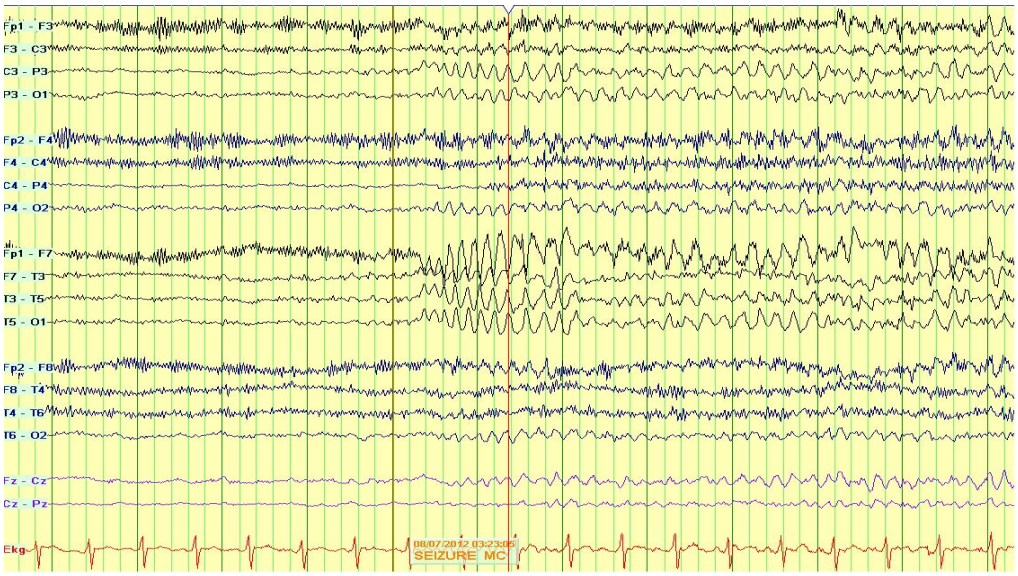

Fig. 1. EEG showing seizure onset characterized by abrupt appearance of rhythmic theta frequency waveforms in the left and right temporal area with rapid secondary generalization.

Most studies evaluating the cardiac effects of lamotrigine though reported no such effects when it is used in conventional anticonvulsant dosing or as a mood stabilizer. Theoretically speaking in overdose, it carries an arrhythmogenic risk and this should be borne in mind when confronted with a patient of lamotrigine overdose. Bupropion is a dopamine and norepinephrine reuptake inhibitor and also causes release of both dopamine and norepinephrine. It is metabolized in the liver into several active metabolites. The inactive metabolites are eliminated through excretion in urine. Seizure is a common side-effect of bupropion and was responsible for its initial withdrawal from the market. The risk of seizure is dose dependent with doses higher than 600 mg more commonly resulting in seizures. The effect of bupropion on the pharmacokinetics of lamotrigine has generated conflicting results with some studies reporting no clinically relevant change and others reporting that low dose bupropion significantly enhances the anticonvulsant activity of lamotrigine (3,4).

Sirianni et al. (5) reported a patient presenting after bupropion and lamotrigine intentional overdose. Approximately 10 hours after ingestion their patient had a generalized tonic clonic seizure followed by rapid cardiovascular collapse characterized by a pulseless wide-complex rhythm requiring advanced cardiac life support in the form of chest compressions, electrical defibrillations, multiple epinephrine boluses and finally an intravenous bolus of lipid emulsion (Intralipid) which acted as a “lipid sink” drawing tissue bound drug off cellular receptor sites and into the plasma thus effectively trapping it. Our patient had QTc prolongation (QT=414 ms, QTc 498 ms) but suffered no cardiovascular collapse (Torsades des Pointes). As the exact time and quantity of bupropion XL and lamotrigine ingested was unclear and our patient was cardiovascularly stable, charcoal administration and intravenous lipid emulsion were not considered necessary and a decision to closely monitor her in the step-down unit was made. Instead our patient went into delayed status epilepticus requiring benzodiazepine administration. Seizures were generalized tonic clonic but exceedingly short in duration and theoretically could have been missed if continuous EEG monitoring was not carried out. Our case highlights the importance of closely monitoring patients presenting with bupropion and lamotrigine intentional overdose as both cardiotoxicity and delayed neurotoxicity in the form of status epilepticus is possible due to unpredictable pharmacokinetics.

References

1. French LK, McKeown NJ, Hendrickson RG. Complete heart block and death following lamotrigine overdose. Clin Toxicol (Phila) 2011; 49: 330-333.
2. Herold TJ. Lamotrigine as a possible cause of QRS prolongation in a patient with known seizure disorder. CJEM 2006; 8: 361-364.
3. Barczyński B, Buszewicz G, Łuszczki JJ, et al. Low dose of bupropion significantly enhances the anticonvulsant activity of felbamate, lamotrigine and topiramate in mice. Eur J Pharmacol 2011; 650: 550-555.
4. Odishaw J, Chen C. Effects of steady-state bupropion on the pharmacokinetics of lamotrigine in healthy subjects. Pharmacotherapy 2000; 20: 1448-1453.
5. Sirianni AJ, Osterhoudt KC, Calello DP, et al. Use of lipid emulsion in the resuscitation of a patient with prolonged cardiovascular collapse after overdose of bupropion and lamotrigine. Ann Emerg Med 2008; 51: 412-415.