CASE REPORT

Persistent status epilepticus due to bupropion intoxication

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ABSTRACT

Bupropion is a generally well-tolerated drug and has adverse effects such as headache, dizziness, dry mouth, nausea, constipation, tremor, drowsiness, agitation, insomnia, hallucinations, allergic reactions and seizures. Although seizures have been reported with therapeutic doses of bupropion, there are few reports presenting development of status epilepticus due to bupropion intoxication with different doses. This rare case of persistent status epilepticus due to intoxication with 9 gm bupropion describes a surviving patient after one of the highest ingested dose cited in literature. We indicate that early management is crucial for patients with intoxication with massive doses of bupropion.

Key words: Bupropion; Intoxication; Status epilepticus; Seizures

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INTRODUCTION

Bupropion has recently been introduced as an atypical antidepressant and also for use as an aid in smoking cessation. It is a monocyclic and structurally unique antidepressant.[1] Bupropion exhibits pharmacologic actions unlike tricyclic antidepressants or selective serotonin reuptake inhibitors. It is known that bupropion is a selective inhibitor of norepinephrine, dopamine and minimally serotonin reuptake. It also has anticholinergic activity. Its mechanism of action in smoking cessation remains unknown.[1-3]

Bupropion is generally a well-tolerated drug and has adverse effects such as headache, dizziness, dry mouth, nausea, constipation, tremors, drowsiness, agitation, insomnia, hallucinations, allergic reactions and seizures. It is associated with a dose-dependent increased incidence of seizures which occur in 0.1% of patients.[4,5] Seizures may result with therapeutic doses of bupropion.[6] However, there are few reports of status epilepticus due to bupropion intoxication with different doses.[7,8]

In this report, we present a rare case of long term status epilepticus due to one of the highest dose of bupropion cited in literature that was managed in our intensive care unit (ICU) and survived.

CASE REPORT

A 36-year-old woman was admitted to our ICU with headache and somnolence 4 hours after ingestion of thirty 300 mg tablets (a total of 9 gm) of bupropion. It was revealed that bupropion treatment had recently been initiated to facilitate her smoking cessation. Headache and somnolence started approximately 2 hours after ingestion. She was admitted with a Glasgow Coma Score (GCS) of 9 with tonic clonic seizures. Her blood pressure was 100/60 mmHg and the initial electrocardiogram (ECG) showed a sinus rhythm at 92 beats per minute. The body temperature, blood cell count, electrolytes, blood gas analysis and liver and renal function tests were within normal ranges. In the ICU, initial management comprised of administration of 100 gm activated charcoal by a nasogastric tube and 5 mg diazepam IV. Brain computerized tomography scanning was normal at admission. After a decrease in GCS to 6, the patient was intubated and ventilated by mechanical ventilation. Thiopental was administered

at an initial dose of 3 mg/kg/h due to persistence of generalized seizures. Four hours after starting, thiopental dose had to be increased to 4 mg/kg/h and after 8 hours to 5 mg/kg/h. Thiopental was stopped on the second day of admission. Due to the continuation of status epilepticus, thiopental dose was restarted in a dose of 4 mg/kg/h and increased to 5 mg/kg/h. Absence of cerebral lesions was identified by magnetic resonance imaging (MRI) on the third day after admission. Thiopental was stopped again on the third day and because of continuation of seizures, restarted with the same dose again. The seizures recurred immediately after stopping thiopental daily, requiring resumption of thiopental at a dose of 5 mg/kg/h until 7th day of admission. Creatine phosphokinase (CPK) levels were normal. When blood pressure decreased under 90/60 mmHg dopamine was infused with a dose range of 2-10 mcg/kg/min. At 7th day of admission tracheostomy procedure performed under local anesthesia at ICU. A trial of thiopental withdrawal on 10th day was successful and no clinical recurrence of seizures was observed; the absence of subclinical seizures was demonstrated by EEG monitoring. Treatment with phenobarbital and valproic acid was continued for five days after thiopental treatment. The GCS of patient was 15 at 11th day and it was decided to stop mechanical ventilation support after a slight weaning procedure. Tracheostomy tube was removed at 14th day of admission. She was discharged from ICU with a complete recovery.

DISCUSSION

This case report describes a patient with status epilepticus after ingesting 9 g of bupropion and her management in our ICU. In most cases reported earlier, the exposure dose was much lower and was responsible for less severe clinical effects such as generalized seizures, sinus tachycardia and several ECG disorders.[7,9] These adverse effects disappear within hours as the mean elimination half life is 21 hours, and bupropion is metabolized by multiple pathways.[10]

Neurologic effects are commonly observed after bupropion overdose.[7] Seizures are the most clinically important central nervous system effect related to bupropion overdose. Belson et al.[7] indicated that seizures resulting from a bupropion exposure most commonly occurred as a single episode; however, nearly 5% of the patients had a seizure which resulted into status epilepticus. They also report that approximately 40% of patients with seizures did not receive any anticonvulsant. This may be due to the occurrence of the seizures before medical attention or to the short duration of seizures. In our case, the patient had generalized seizures that couldn't be treated with diazepam and progressed rapidly to severe status epilepticus that was controlled only by continuous infusion of 5 mg/kg/h of thiopental sodium. In a case report by Morazin et al,[8] the patient was exposed to a dose of 12 g of bupropion and their patient had status epilepticus as in our case. There are, however, some differences between our case and theirs. First, the admission time after ingestion and second in the thiopental dose. They used thiopental at a rate of 3.5 mg/kg/h, in contrast to 5 mg/kg/h in our case.

In another case report by Skripuletz et al,[6] a 50 years old patient with a bupropion dose of 300 mg/day had been found unconscious with status epilepticus and was successfully treated by diazepam. They indicated that bupropion appears to be effective in ameliorating symptoms of smoking withdrawal, but physicians should be aware that there is an increased risk of seizures and they suggested performing an EEG prior to bupropion administration. Their case showed that a maximal therapeutic dose may also cause status epilepticus in patients with a low threshold of seizure activity, even if there is no over dosage.

The status epilepticus could be assigned to bupropion. Onset of status epilepticus corresponds to the time to peak serum bupropion concentration and it is usually between 2 and 3 hours after the drug ingestion. The severity of the status epilepticus and the difficulties encountered in controlling it are probably related to the massive dose of ingested bupropion and subsequent high cerebral concentrations. However, long intervals after ingestion and the time to initial management may result in aggravated symptoms.[8] Some case reports presented rapid death due to massive bupropion overdose from cardiorespiratory arrest usually due to long intervals between the time of ingestion and the time of initial management.[11,12] In a case report of Harris et al[12] a 26 years old patient after bupropion intoxication with a dose of 23 gm had cardiac arrest and died after 4 days. It is evident that delayed treatment makes the prognosis worst.

This rare case of status epilepticus due to intoxication with 9 gm of bupropion describes survival of a patient after one of the highest ingested dosage. We conclude that prompt management and intensive care of patients with bupropion intoxication with massive doses is crucial for positive outcome.

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