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Generalized Tonic-Clonic Seizure Due to the Concomitant Use of Bupropion Extended-Release and Moxifloxacin

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Abstract

Bupropion extended-release (XL), an amphetamine-like dual mechanism drug, is used for the treatment of major depressive disorder, and its use is associated with a dose-dependent risk of epileptic seizures. Moxifloxacin is synthetic fluoroquinolone antibiotic agent which has proconvulsant side effects. Although there is no drug-drug interaction between these two drugs, their concomitant use can trigger epilepsy. In this report, we discussed a male patient using bupropion XL, who developed generalized tonic-clonic seizure after treatment with moxifloxacin and had no history of seizures. The association of bupropion XL with catecholamines and the association of both bupropion XL and moxifloxacin with gamma aminobutyric acid were possible accused mechanisms. This case report suggests physicians to pay attention to the potential risk of bupropion XL- and moxifloxacin-induced seizures.

1. Introduction

Bupropion extended-release (XL), a unique and effective antidepressant, can result in seizures following overdosing in humans. Although seizures associated with the therapeutic use of bupropion is infrequent, it can be seen (Yang, Yeh, & Liang, 2019; Örüm, Egilmez, & Kalenderoglu, 2018). Moxifloxacin which has a broad spectrum of antibacterial activity is included in the fluoroquinolones. Central nervous system (CNS) side effects of fluoroquinolones occur at an overall incidence of 1%–2%. Moxifloxacin reveals less potential for causing CNS-related side effects compared with other fluoroquinolones (Qiao, Cui, & Li, 2011; Shi & Xu, 2014; Cone & Horowitz, 2015). Although reports of seizures related to the use of bupropion XL at therapeutic doses are rare, seizures due to moxifloxacin have been reported even more rarely. According to our best knowledge, there is no report of seizure in the patient who was started moxifloxacin while using bupropion XL. Herein, we present a male patient using bupropion XL, who developed generalized tonic-clonic seizure (GTC-S) after treatment with moxifloxacin and had no history of seizures.

2. Case Presentation

A 29-year-old, 60-kg, doctor of medicine male was hospitalized with GTC-S. He was being followed up at a psychiatry outpatient clinic for 1 years with a diagnosis of major depressive disorder. Sertraline 100 mg/day per oral (PO) which was started a year ago was discontinued 20 days ago due to sedation and he was managed by bupropion XL 150 mg/day PO. Four days before admission, moxifloxacin 400 mg/day PO was initiated with the diagnosis of community-acquired pneumonia (CAP). On the day of admission, after a fast paced 30-minute run, he collapsed on the ground and began to have a two-minute seizure. The patient's thyroid, kidney and liver function tests were within normal limits. The fasting blood glucose, protein level and lipid profile were within normal limits. Chest X-ray, electrocardiogram, computed tomography, and magnetic resonance imaging gave normal results. Electroencephalography was unremarkable. The relatives of patient stated that there was no change in dietary and fluid intake in recent days. The patient had no drug use other than bupropion XL and moxifloxacin. His medical history included a surgery for gall bladder but no previous history of seizure. He had no systemic disease such as hypertension or diabetes mellitus. He consumed alcohol and had smoking. No allergies to drugs, foods and pollens were reported. Family history was unremarkable. His family history was unremarkable apart from diabetes mellitus type 2 in his mother. The seizure was attributed to bupropion XL, moxifloxacin or their common effects. Both drugs were stopped and ceftriaxone 0.5 g/day intramuscularly was started for CAP. No similar side effects were observed after one-week follow-up. Sertraline 25 mg/day was started and titrated to 50 mg/day after two weeks. The patients and their relatives were informed about the effects and possible side effects of the treatment. At the end of three months, sertraline 200 mg/day significantly decreased his psychiatric complaints and he was managed with modafinil 200 mg/day for sedation. The patient and his relatives were warned about seizure due to bupropion XL/moxifloxacin use and the informed written consent has obtained from them for publication.

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3. Discussion

There is no drug-drug interaction between bupropion XL and moxifloxacin. However, these two drugs have proconvulsant properties (Yang et al., 2019; Shi & Xu, 2014). In this case, it was thought that the seizure was caused by the accumulation of proconvulsant effects of these two drugs.

Bupropion and its active metabolite, hydroxybupropion, acts via inhibition of norepinephrine and dopamine reuptake. Bupropion's sympathomimetic amine structure may also suggest possible stimulation of the hypothalamus to release catecholamines into the central nervous system (Yang et al., 2019). This may be a possible cause of seizure in our patient. However, bupropion XL indicates a greater potential dose-related seizure than other antidepressants. The mean ingested daily dose of bupropion XL in patients who had seizures was reported as 8.3 mg/kg of body weight. Our patient was relatively weak (body mass index 18.5) and this value was 2.5 mg/kg (Shah & Hirsch, 2001). In other words, it cannot be said that there will be no side effects with low dose bupropion XL. Another problem with bupropion XL-induced seizures is the delayed onset (Starr et al., 2009). Mishra, Sardesai & Rastogi (2017) reported a seizure secondary to bupropion XL 300 mg/day in the seventh weeks. Second possible cause of the seizure in our patient is the use of moxifloxacin (Cone & Horowitz, 2015).

The exact mechanism by which moxifloxacin induce seizures remains to be elucidated, but it can be related to the chemical structure of the fluoroquinolones. Lipophilicity of a compound may affect the extent of its penetration into the CNS, and thus affects the risk of CNS adverse effects (Domagala, 1994). Fluoroquinolones appear to displace GABA or compete with GABA binding at the receptor sites within the CNS, resulting in stimulation (Akahane, Sekiguchi, Une, & Osada, 1989). Moxifloxacin is highly hydrophilic and lipophilic, penetrates well through the blood brain barrier, but shows low excitatory potency compared with other fluoroquinolones (Domagala, 1994). In addition to the chemical properties of the fluoroquinolones, fluoroquinolone-related seizures are most likely to occur in a susceptible population with predisposing factors, such as electrolyte imbalances, pre-existing epilepsy, trauma, or concomitant use of proconvulsant drugs (Qiao et al., 2011; Shi & Xu, 2014; Cone & Horowitz, 2015). In our study, the last one of these risk factors was presented. Shi and Xu (2014) reported moxifloxacin-induced seizure in the six day of administration. In our case, the time of onset of seizure was consistent with the literature of time of both bupropion and moxifloxacin-related seizure onset.

One of the mechanisms responsible for the suppression of seizures in humans is the strengthening of GABA inhibition (Shi & Xu, 2014; Cone & Horowitz, 2015). Low GABA levels frequently accompany MDD. Regardless of treatment, depressive symptoms in our patient may have lowered GABA levels and may have led to seizure susceptibility (Wang, Wang, Zheng, & Zhang, 2018). Bupropion is a nicotine agonist and nicotine stimulates the release of GABA. GABA derivatives are partly relative to inhibition of the dopaminergic system. The receptor dopamine 2 (D2) mediates anticonvulsant action and bupropion acts on D2 receptors. Decreased D_2 activity may have

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predisposed to seizure (Beard, Shahab, Cummings, Michie, & West, 2016; Chen, 2006).

In conclusion, bupropion XL and moxifloxacin lowers the seizure threshold, it should be used cautiously with together and with other medications that also lower seizure threshold. This case report suggests physicians to pay attention to the potential risk of bupropion XL- and moxifloxacin-induced seizures, especially in patients with lower body weight.

Conflict of interest

No conflict of interest was declared by the authors.

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