

# Mania possibly linked with bupropion for smoking cessation: A case report

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**How to cite:** Dwyer S, Hieber R. Mania possibly linked with bupropion for smoking cessation: A case report. *Ment Health Clin* [Internet]. 2016;6(6):314-7. DOI: 10.9740/mhc.2016.11.314.

## Abstract

Bupropion is an antidepressant thought to have a reduced risk of inducing mood switching as compared to other antidepressants. Minimal information is available on the induction of mood shifts when used for smoking cessation. This case describes a 38-year-old female who experienced mania following initiation of bupropion for smoking cessation. After completion of a thorough literature search, this appears to be the first case report describing mania induced by bupropion that was refractory to medications and was resolved with electroconvulsive therapy. This case highlights the need for clinicians to perform thorough histories of patients to avoid missing psychiatric history prior to starting bupropion as well as monitor for changes in mood or behavior after initiation of therapy.

**Keywords:** mania, hypomania, bupropion, smoking cessation, tobacco cessation, electroconvulsive therapy

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**Disclosures:** The authors have no potential or actual conflicts of interest regarding this case report.

disorder. Additionally, electroconvulsive therapy (ECT) has been shown to achieve remission in 60%–80% of acutely manic patients, but the evidence of ECT in mania refractory to medication therapy is limited.<sup>3</sup> In this case report, a female patient who experienced mania following initiation of bupropion for nicotine dependence is described, and a literature review is provided.

## Background

Bupropion is a dopamine/norepinephrine reuptake inhibitor that is FDA approved for the treatment of smoking cessation. Although the exact mechanism is not fully understood, the therapeutic effects of bupropion are thought to be due to inhibition of presynaptic dopamine and serotonin reuptake transporters and possible antagonism of nicotinic acetylcholine receptors.<sup>1</sup> Although antidepressant therapy is not generally recommended in bipolar disorder, bupropion is thought to have a reduced risk of inducing mood shifts compared to other antidepressants when used for the treatment of depression in bipolar patients.<sup>2</sup> Minimal information is available on the induction of mood shifts when bupropion is used for smoking cessation in patients without a history of bipolar

## Case

A 38-year-old African American female presented to the emergency department for chest pain. The patient's past medical history was significant for hypertension, for which she had not taken her lisinopril for about 2 years, and diabetes, controlled with diet. Additionally, the patient had a history of smoking for 20 years and had quit about 3 months prior to admission; however, 1 week prior to the onset of chest pain, the patient was started on oral bupropion 150 mg every morning for smoking cessation for tobacco cravings. In the emergency department, the patient received aspirin chewable 162 mg by mouth and 3 sublingual nitroglycerin tablets, which relieved the chest pain, and was admitted to the general medicine floor in order to rule out an acute coronary syndrome. The next

day, prior to her stress test, the patient went to the cardiology clinic, where she became confused and began talking about demons and auras. The patient's husband noted that this behavior was strange, and the patient was escorted back to the medical unit. On the medical floor, the patient was requesting to be examined by a female because having a male examine her would be "inappropriate" because "together (they) are the body of Christ."

The patient was evaluated by psychiatry, and the patient's husband provided further insight into the patient's bizarre behavior. According to the patient's husband, the patient started acting strange when she woke up the morning before coming to the emergency department. She was hyperverbal, religiously preoccupied, and distracted with flight of ideas. The husband also reported that the patient had similar manic symptoms about 5 years prior after using cannabis and was hospitalized for a brief period at a private hospital. Per the husband, the symptoms resolved, and the patient was discharged with a diagnosis of schizophrenia. The patient was treated with oxcarbazepine 300 mg per day, risperidone 1 mg twice daily, and fluoxetine 20 mg daily, and it appears that the patient took these medications for approximately 6 months following this previous hospitalization. Because of the current sudden changes in mood, the patient was admitted to the inpatient mental health floor for mood stabilization. While in the inpatient psychiatry unit, the patient continued to exhibit behaviors consistent with manic delirium, such as agitation, hypersexuality, and combativeness, requiring multiple doses of intramuscular haloperidol 5 mg and lorazepam 4 mg, given as needed. The patient was started on lithium 600 mg twice daily, and appropriately drawn lithium trough levels increased up to 1.74 mEq/L due to acute worsening of renal function. However, the patient was without side effects or any resolution of symptoms. The patient's mania and psychosis continued to worsen despite trials of haloperidol 10 mg twice daily and risperidone 1 mg at bedtime, and ultimately the patient required restraints as she was no longer responding to intramuscular haloperidol 10 mg, lorazepam 2 mg, or olanzapine 10 mg. After 10 days of admission on the mental health unit, lack of response, and dangerous behaviors, the psychiatry team resolved to perform emergency ECT. After the first ECT treatment, the patient remained agitated and delusional and continued to require restraints and as needed haloperidol and lorazepam. She received her second treatment of ECT the following day, which she tolerated.

The psychiatry team resolved to admit the patient to the intensive care unit (ICU) for sedation to avoid injury with a goal of 24 hours without restraints and intravenous medications before being transferred back to inpatient psychiatry. The patient was admitted and placed on a dexmedetomidine infusion with haloperidol and loraze-

pam as needed for agitation, which the patient continued to need during the initial ICU course. The patient's third ECT resulted in some improvement in her behaviors. The patient remained in the ICU for a total of 6 days, and during the last 2 days of the ICU stay, the patient was not sedated and did not require any medication or restraints. The patient was stable and not psychotic or manic, so she was discharged home after her fourth ECT with instructions to follow up with outpatient psychiatry. Postdischarge, the patient received 4 more ECT treatments. Three months postdischarge and 2 months post-ECT, the patient remained stable without any pharmacologic treatment and only psychotherapy.

## Literature Search

A literature search was conducted through PubMed using the following MeSH terms: "bupropion," "bipolar disorder," and "smoking cessation." Results written in English were included. The initial search used "bupropion" and "bipolar disorder," which yielded 76 articles that were reviewed for case reports discussing bupropion-induced mania and hypomania. An additional literature search was conducted adding "smoking cessation" to determine if previous literature was available regarding bupropion-induced mania when used for smoking cessation rather than treatment of bipolar depression. This search produced 10 reviewable articles. For review of ECT treatment in mania, a PubMed search using MeSH terms "electroconvulsive therapy," "bipolar disorder," and "delirium" was conducted, and it yielded 21 results. Results written in English were included.

## Discussion

### Bupropion-Induced Mood Shift

Bupropion, compared with other antidepressants, is thought to have a reduced risk of inducing mood shifts.<sup>4</sup> Additionally, it has been reported that the severity of symptoms is less with bupropion-induced mood shifts compared to other antidepressants. However, there have still been reports of bupropion-induced mood shifts when used for depression in patients with bipolar disorder. Aggarwal and Sharma<sup>5</sup> described two separate cases of bupropion-induced mood switch, 1 in a patient with bipolar I depression and 1 with bipolar II depression. The patient with bipolar I depression was receiving bupropion that was titrated to 300 mg/d in 5 days. After 2 weeks, the patient complained of decreased sleep over 2 days and then switched to irritable mania. The patient with bipolar II depression was taking bupropion 150 mg for 3 days, followed by 150 mg twice daily. After 3 weeks, the patient switched to hypomania. In both cases, symptoms resolved upon discontinuation of bupropion. Goren and Levin<sup>6</sup>

described a case of a male with bipolar affective disorder who was treated with bupropion for depression. In this particular case, the patient did not experience manic symptoms until a few days after titration to bupropion 600 mg/d. These reports certainly support the necessity for close monitoring for mood switches in patients with a known diagnosis of bipolar disorder treated with bupropion for depression.

To the best of our knowledge, there are only 2 previously published case reports<sup>7,8</sup> describing bupropion-associated mood switches when used for the treatment of nicotine dependence, and only 1 of these reports describes the mood switch after bupropion initiation. Giasson-Gariepy et al<sup>7</sup> described a case involving a male patient started on bupropion for nicotine dependence while also taking other mood-stabilizing medications. This patient developed hypomanic symptoms with treatment initiation, and the symptoms became more pronounced when the dose was increased on the fourth day of therapy. This patient had a previous diagnosis of dysthymic disorder maintained on venlafaxine and quetiapine and a history of substance abuse. A possible drug interaction between bupropion and venlafaxine was discussed as a possible contributor to the mood shift. The patient's hypomanic symptoms resolved following discontinuation of bupropion. Michael et al<sup>8</sup> described a case report of a patient exhibiting manic symptoms following discontinuation of bupropion therapy for smoking cessation. The patient was taking bupropion 300 mg/d for 5 weeks but was still not able to stop smoking. As a result, the patient abruptly stopped taking bupropion and developed manic symptoms 2 weeks later. The acute mania was initially managed with haloperidol, then switched to risperidone due to development of severe akathisia. The acute mania resolved in 16 days.

A recently published double-blind, randomized, placebo-controlled clinical trial assessed the safety of bupropion in smokers both with and without psychiatric disorders.<sup>9</sup> Anthenelli et al<sup>9</sup> found that of the 989 patients receiving bupropion for smoking cessation who did not have any psychiatric history, only 1 patient (0.1%) experienced mania, and this was of moderate intensity. No patients experienced severe mania. Of the 1017 patients with a significant psychiatric history receiving bupropion for smoking cessation, 9 patients (0.9%) developed mania with only 1 patient (0.1%) experiencing severe mania. Based on this clinical trial, it appears that mania from bupropion, regardless of the presence of significant psychiatric history, is rare when used for smoking cessation. In this trial, the 2 most common adverse effects associated with bupropion therapy were agitation and panic.

## ECT Treatment for Mania

Electroconvulsive therapy has been previously reported to be effective in the treatment of mania and manic

delirium.<sup>3,10-13</sup> Danivas et al<sup>10</sup> described 2 case reports involving effective ECT in the treatment of manic delirium. The first patient was a 17-year-old female, who was initially started on olanzapine 10 mg/d. The patient was admitted again 20 days later due to worsening symptoms and wandering behavior. She was successfully sedated with lorazepam and haloperidol during periods of excitement and was empirically started on ECT. By the end of 6 ECT sessions, the patient was euthymic and started on lithium 900 mg/d. The second patient was a 19-year-old male who presented with manic symptoms that were not improving with intravenous lorazepam. The patient was started on ECT and started to show improvement after the second ECT session. After 6 sessions of ECT, this patient also achieved euthymia and was started on olanzapine 10 mg/d. In our patient, the manic symptoms were refractory to haloperidol, lithium, lorazepam, olanzapine, and risperidone. The patient received 4 ECT sessions while an inpatient and then weekly ECT sessions for 4 weeks as an outpatient. The patient remained euthymic for 2 months after her last ECT without any maintenance medications.

The case described in this report depicts a patient experiencing a mood switch after initiating bupropion for smoking cessation without being on another mood-stabilizing agent. Additionally, this appears to be the first case report involving manic symptoms resistant to multiple standard medications that was finally resolved with ECT. This patient did have a history of cannabis-induced psychosis, and the association of cannabis and mania is described elsewhere.<sup>14</sup> However, this episode occurred 5 years earlier, and the patient and spouse did not report any continuing symptoms. The onset of this patient's manic symptoms occurred approximately 1 week following initiation of bupropion therapy, which suggests a bupropion-induced mood shift in this patient. The calculated Naranjo Adverse Drug Reaction Probability score for this case is 5, making it probable that the mania was due to bupropion. Additionally, this case report demonstrates the potential effectiveness of ECT in mania that is unresponsive to medications.

## Conclusions

Patients with significant psychiatric history not maintained with mood-stabilizing agents may be at risk for mood shifts from bupropion when used for the treatment of nicotine dependence. This case report suggests the importance of carefully monitoring patients for mood shifts when using bupropion for smoking cessation regardless of whether or not the patient is taking other mood-stabilizing agents at the time of bupropion initiation. This case highlights the possibilities of missing psychiatric history and the resulting adverse reaction to

bupropion. Thorough patient counseling should be performed at the time of bupropion initiation, instructing patients to report changes in their mood or behaviors.

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