Bupropion-Induced Mania and Hypomania: A Report of Two Cases

To the Editor: In treating bipolar depression, bupropion has been considered to carry much less risk of switching into hypomania/mania, which should be still less when it is prescribed with lithium. However, despite this, we report on two patients, one with bipolar I depression and another with bipolar II depression, who switched to mania and hypomania, respectively, while being treated with bupropion alone or in combination with lithium. Both patients achieved remission with atypical antipsychotics, lithium, and clonazepam.

Treatment with antidepressants is common in bipolar patients,[1] and antidepressants do have a role in the treatment of bipolar depression, although with caution.[2] Bupropion is a selective catecholamine (norepinephrine and dopamine) reuptake inhibitor.[3] Compared with other antidepressants, it is the preferred choice in the treatment of bipolar depression because of its low propensity for switching into mania/hypomania (treatment-emergent affective switch).[4–6] However, we report two patients with bipolar depression who switched to hypomania and mania while taking bupropion alone or as an adjunct to lithium, which speaks against the lesser switching potential of bupropion in bipolar depression.

Case Report I

A 26-year-old man diagnosed with bipolar disorder who was maintained on sustained-release lithium 900 mg/day (level: 0.6 meq/liter) presented with symptoms of breakthrough depression characterized by sad mood, anhedonia, anergia, and depressive ideation for 2–3 weeks. Family history of bipolar disorder was present. History of substance misuse was absent, but the patient had a manic switch while he was on fluoxetine monotherapy for bipolar depression. In view of this background, it was thought to add bupropion to prophylactic lithium so that the risk of treatment-emergent hypomania/mania could be minimized. Bupropion sustained-release was titrated to 300 mg/day after 5 days. After about 2 weeks, the patient complained of decreased sleep for 2 days and then switched to irritable mania, characterized by irritable mood, decreased need for sleep, pressured speech, distractibility, and psychomotor agitation. The symptoms were controlled with lithium 1,200 mg/day (level: 0.9 meq/liter), olanzapine 20 mg/day, quetiapine 200 mg/day, and clonazepam 2 mg/day. The patient achieved euthymic status after about 6 weeks; his medications, except lithium, were tapered off gradually. Now he is maintaining remission with lithium for the last 1 month.

Case Report II

A 22-year-old man diagnosed with hypomania in remission and off medication presented with depressive symptoms characterized by sad mood, anhedonia, anergia, lethargy, decreased appetite, and increased sleep for the last fortnight. There was no history of substance misuse or family history of affective disorder; however, history of alcohol dependence syndrome was positive in the patient's uncle. The patient was diagnosed with DSM-IV-TR bipolar II depression and was prescribed bupropion sustained-release, 150 mg/day, which was increased to 150 mg bid after 3 days. After about 3 weeks, the patient switched to hypomania characterized by euphoria, voluble speech, decreased need for sleep, overactivity, grandiosity, and increased sexual attraction to girls. His symptoms were controlled with lithium 900 mg/day, olanzapine 10 mg/day, and clonazepam 0.5 mg/day, and he achieved euthymia after 4 weeks. All medications except lithium were tapered off gradually, and the patient is in remission now for the last 2 months.

Discussion

Patients developing mania/hypomania with the use of antidepressants for depressive disorder have been labeled as bipolar type III disorder, a new subtype beyond DSM-IV and ICD-10 categories. The French EPIDEP study has shown that in such patients there is a family history of bipolar disorder or temperament.[7,8]

The first case, a BP-I patient, had a past history of manic switch with fluoxetine (without concurrent mood stabilizer) and positive family history of bipolar disorder and hence was quite prone for affective switch. The patient switched to mania while taking bupropion as an adjunct to lithium. Some case reports have also observed bupropion-induced mania with standard or higher doses.[9,10] However, unlike the present case, addition of bupropion to mood-stabilizer therapy has not been shown to increase the risk of cycling from depression to mania or hypomania in a large Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) clinical trial.[11]

In comparison to BP I, Bipolar II-disorder patients are found to be less prone to antidepressant-emergent mania/hypomania switch.[12] The second case, a first-time diagnosed BP-II depression with negative family history of bipolar disorder, developed hypomania after bupropion therapy was instituted. In both cases, bupropion appears to have triggered the manic/hypomanic switch, and such switching has occurred even in the presence of lithium. Although these two case reports cannot overrule the findings of larger studies or the possibility of spontaneous occurrence of mania/hypomania, they still call for judicious use of bupropion in patients with bipolar depression.

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