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Case Report Open Access

Bupropion-Induced Psychotic Mania: Risk Factor, Clinical Course and Dosage

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Abstract

Bupropion is a dopamine/norepinephrine reuptake inhibitor and considered to carry a much lower risk of inducing mood shift compared with other antidepressants. We described here a patient who experienced the first episode of mania with psychotic features after escalating the dose of bupropion in the treatment of major depression disorder. Miss C is a 40-year-old female, who was diagnosed major depressive disorder with melancholic features and received bupropion 150 mg daily. The dose of bupropion was escalated to 300 mg daily due to the incomplete response. Three days later, she dramatically exhibited elated mood, hostility, irritability, hyper-talkative, hyper-activity, hyper-sexuality, marked delusion of religion, persecution, and grandiosity. The manic symptoms were subsided after discontinuation of bupropion immediately and prescribed quetiapine 300 mg daily within one week. The risk factors for mood shift including iron deficient anemia, melancholic features, clinical course, and the dosage of bupropion is discussed.

Keywords: Bupropion; Psychotic mania; Depression

Introduction

Bupropion is a dopamine/norepinephrine reuptake inhibitor and is usually considered to carry a lower risk of mood shift than other antidepressants [1]. There are few published case reports of bupropion-related mania or hypomania in the treatment of bipolar depression [2], and major depressive disorder [3,4]. We describe herein a patient who experienced a first episode of mania with psychotic features after escalating the dose of bupropion in the treatment of major depressive disorder. To the best of our knowledge, this is the first case report of bupropion-related mania with psychotic features in a patient with the diagnosis of major depressive disorder. The risk factors for mood shift, including melancholic features, clinical course, iron-deficient anemia and the dosage of bupropion, are discussed.

Case Report

Miss C, a 40-year-old divorced female with a normal birth and developmental history, denied any past psychiatric disorders or systemic diseases. She had maintained a good occupational performance and fair interpersonal relationships in the past. However, one month before hospitalization, she experienced a gradually depressed mood (especially worse in the morning), psychomotor retardation, anhedonia, impaired concentration, early morning awakeness, difficulty in falling asleep, and severe guilty feelings. Meanwhile her occupational functioning was also deteriorating. At admission, no delusions or hallucinations were found. The patient reported no previous symptoms of mania/hypomania and there was no family history of mood disorders. She was diagnosed with major depressive disorder with melancholic features, based on the DSM-IV-TR. Physical examination and routine laboratory investigations, including cell blood count, biochemistry and thyroid function, were all within normal limits, except that the hemoglobin was 9.3 g/dl which was later proved to be iron-deficiency anemia. The Montgomery–Åsberg Depression Rating Scale (MADRS) at admission was 28. Bupropion (Wellbutrin XL®) 150 mg daily was initially prescribed. Her mood and energy showed mild improvement in the first 6 days. Hence, the dose of bupropion was escalated to 300 mg daily due to the incomplete response. Three days after escalation of bupropion, she developed insomnia, and thereafter, she dramatically exhibited an elated mood, hostility, irritability, hyper-talkativeness, hyper-activity, hyper-sexuality, and marked delusions of religion, persecution, and grandiosity. Her diagnosis was revised to manic episode with psychotic features, with a score of 29 on the Young Mania Rating Scales (YMRS). Bupropion was discontinued immediately and quetiapine (Seroquel XR®) 300 mg daily was initiated. Symptoms as hostility, agitation, and irritability were largely improved within 3 days; hyper-talkativeness and delusions of religion, persecution and grandiosity disappeared since 5 days after discontinuation of bupropion.

Discussion

The temporal relationship between medication and manic symptoms in our case suggests that the manic episode with psychotic features could be attributed to bupropion. This observation is further supported by the Naranjo scale score of 9. In our case, the initial diagnosis was drug-naïve first-episode major depressive disorder, with no past history of manic symptoms. The shifting mood with psychotic features immediately followed the escalation of the dose of bupropion, which supported the idea of a bupropion-related psychotic manic episode.

Bupropion, as a dopamine transporter (DAT) inhibitor and norepinephrine transporter (NET) inhibitor, is very similar to cocaine as a typical dopamine transporter (DAT) inhibitor and also similar to methylphenidate as a DAT inhibitor and a dopamine releaser [5]. It is also structurally related to cathinone and cocaine, which both are stimulant [6]. As a potential stimulant, previous literature documented the side effect of manic or psychotic symptoms [6-8].

Compared with previous cases, and aside from the mechanism of dopamine/norepinephrine reuptake inhibitor, we assumed there were two vulnerability factors that might explain why this case with major depressive disorder shifted to mania with psychotic features shortly after escalating the dose of bupropion. First, several previous studies have documented that the clinical picture of melancholic depression is considered to be more closely aligned with the depressive and/or mixed phase of bipolar disorder than unipolar depression [9]. The core symptoms of melancholic features may explain why, eventually, the patient developed a manic episode. Our case supports this idea of the role of melancholic symptoms in predicting the diagnosis of bipolar disorder. Second, the moderately decreased hemoglobin (iron-deficiency anemia, IDA) may also have contributed to the mood shift to some extent. Iron plays an important role in the oxygenation of brain parenchyma and works as a co-enzyme in the synthesis of many neurotransmitters. Lack of iron also may cause abnormal myelination of white matter and is implicated in dopamine function, which has potential relevance for mood disorder [10]. Chen et al. recently presents a close connection between IDA and bipolar (odds ratio=6.05) or unipolar depression (odds ratio=2.89) in adolescent patients, respectively [11]. Robert et al. also reports an association between low serum ferritin level and depressive symptoms, which supports the important role of iron in mood disorders.

In this case, bupropion 300 mg daily triggered the manic episode. Golden et al. reported a patient that experienced a recurrence of psychotic symptoms when re-challenged with bupropion 300 mg daily. Nevertheless, decreasing the dosage to 200 mg daily resulted in adequate symptom control without recurrence of psychotic symptoms [12]. A similar condition may explain the dose-dependent effect on manic episodes in our case, which showed manic symptoms with psychotic features at 300 mg daily and relatively acceptable symptom control without manic symptoms at 150 mg daily. The triggering of manic symptoms by bupropion in a dose-dependent manner was also documented in another report which suggested that doses above 450 mg daily had a high propensity for triggering manic symptoms [13].

In conclusion, this case highlights the fact that the characteristics of bupropion is a potential stimulant, even through this drug has been usually considered to be a low risk antidepressant for mood shift. We need to be cautious for mood shifts when prescribing antidepressants to patients with depressive disorder with melancholic features.

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