

Case report

**Can lamotrigine induce a switch into mania?**

Elie Cheniaux\*

Allan Dias\*

José Luiz M.Lessa\*

Marcio Versiani\*

\*Anxiety and Depression Research Programm, Bipolar Disorder Studies, Institute of Psychiatry,  
Federal University of Rio de Janeiro (UFRJ), RJ, Brazil.

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## INTRODUCTION

The treatment of bipolar depression (BD) has not received as much attention as the treatment of mania or unipolar depression.<sup>1,2</sup> So far, no single antidepressant has proved efficacy in the treatment of BD in at least two controlled clinical trials performed.<sup>3</sup> Moreover, there is always a concern that antidepressants may cause a manic switch in bipolar patients, especially the tricyclic drugs.<sup>4</sup> On the other hand, mood stabilizers (among them lithium, carbamazepine and valproate) seem to be more effective in mania than in depression<sup>5</sup> and they are associated to a significant worsening of cognitive performance.<sup>6</sup>

Lamotrigine is an anticonvulsant that has been employed in the treatment of bipolar disorder (BPD). Many clinical trials indicate that, although lamotrigine is not effective in acute mania nor in the prevention of manic episodes, it is helpful in the acute phase of BD and in the prophylaxis of future depressive episodes.<sup>7,8</sup>

A major benefit with the use of lamotrigine in BD is that, although it has an antidepressant activity, it is associated to a low rate of manic switch or hypomania, even during monotherapy. In the study developed by Calabrese et al.,<sup>5</sup> only 5.4% of depressed bipolar patients taking lamotrigine had a switch, as compared to the 4.6% who were given placebo, a non-significant difference. In the 52-week, open-label study of lamotrigine as maintenance treatment of depression in bipolar patients, carried out by McElroy et al.,<sup>9</sup> patients had less manic or hypomanic episodes than the year before. Another important characteristic of lamotrigine is that it seems not to affect cognition.<sup>6,10</sup> On the other hand, this drug has been associated with an increased risk of rashes, which are in general benign, but sometimes may be life-threatening.<sup>11</sup>

## CASE REPORT

The patient is natural from Rio de Janeiro, where he lives; he is divorced, graduated and works as a civil servant in one of the most important public institutions in the country. In November 2000, at the age of 35, he got a leave to carry out a doctorate degree. Up to that moment, he had

already presented several depressive and hypomanic episodes, the first one at the age of 14, but he had never been admitted to a psychiatric institution. At that time, the diagnosis was BPD type II.

Between November 2000 and August 2001, the patient was taking lithium and fluoxetine (sometimes associated with nortriptyline). During this period, the depressive symptoms showed great fluctuation; he had some asymptomatic periods intermingled with significant aggravations, presenting even suicidal ideation. In August 2001, when he “switched” his status into hypomania, all drugs were withdrawn and replaced by monotherapy with divalproate. In December 2001, he interrupted treatment on his own, which he had been following irregularly, because he complained about the excessive sedative effect of the drug and difficulties in concentration and thinking.

Between December 2001 and November 2004, the patient decided not to take any psychiatric drug. During this period, he became a rapid cyler, presenting many depressive episodes, certainly more than 10 a year, which showed mild to moderate intensity, and lasted in average only 4 days. Hypomania episodes were rare and very short, sometimes lasting from only a few hours, to a maximum of 1 or 2 days. He did not conclude his doctorate, but, despite the frequent depressive episodes, he came back to work, where he reached a managing position, performing it successfully. Sometimes he did not go to work or arrived late, but once depression was over, he returned to his normal rhythm of work. In November 2004, he was then 39, the depressive episodes became more frequent, and the patient decided to take medication again. However, he did not admit taking lithium or divalproate, justifying that they impaired his intellectual performance, which was essential in his professional activities.

Monotherapy with lamotrigine 12.5 mg/day in alternated days was prescribed. After two days, the dosage was 25 mg/day and the patient had a significant amelioration of depressive symptoms and no side effect at all, and he became quite confident on the treatment. In the following month, December, the dosage was at 50 mg/day and after 10 days, the patient entered what seemed to be a manic episode. He showed irritability, became arrogant and suspicious – though not delusional – started to spend much money and had his sexual drive substantially increased.

Medication was discontinued and about 15 days later all symptoms remitted. In March 2005 he was not taking any psychotropic drug and presented a new depressive episode.

## DISCUSSION

In BPD II, the management of depressive episodes is of paramount importance, as they are more frequent, long and severe than the episodes of hypomania.<sup>3</sup> Moreover, in this mental disorder, the risk of suicide is higher than in unipolar depression or in BPD I.<sup>2</sup>

According to some therapeutic guidelines designed by international specialists, in the less severe cases of BD, lithium in monotherapy must be used. In the most severe cases, the first alternative must be the association of a mood stabilizer with an antidepressant. The most indicated mood stabilizers are lithium and lamotrigine, but valproate and carbamazepine may also be used. Among antidepressants, the preference is for selective serotonin reuptake inhibitors, bupropion and venlafaxine, which would not induce a switch into mania as frequent as others.<sup>1,3,12,13</sup>

It is not known if the depressive episodes in BPD II respond to medications the same way as in BPD I.<sup>2</sup> There are no controlled studies about the management of depression in bipolar II patients, and open studies are still scarce in the literature. In the open studies reviewed, we found positive responses with fluoxetine,<sup>14,15</sup> venlafaxine<sup>16</sup> and also with lamotrigine.<sup>17</sup>

The case reported here, lamotrigine, corresponding to our expectations, improved the depressive symptoms with no side effects as to cognition. Surprisingly, however, its prescription was associated with a manic switch. It is not possible to assure that lamotrigine was the cause of this event, provided that it can occur even with placebo. Besides, there may have been a coincidence: a manic episode could have taken place even if the patient had not taken any medication, it could have been only part of the natural course of his illness. But we consider that, at least in this patient – and maybe in other cases of bipolarity – it may be safer to avoid the prescription of lamotrigine alone, using it preferably in association with another mood stabilizer, as lithium, valproate or carbamazepine.

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#### **ABSTRACT**

*Controlled clinical trials involving bipolar patients have shown that lamotrigine is effective in acute phase treatment of depression and mainly in the prevention of new depressive episodes. We report the case of a bipolar II, rapid cycling patient who used lamotrigine (in monotherapy) during a depressive episode and developed a dysphoric manic episode. This episode resolved soon after*

*discontinuation of the drug and was followed by a new depressive episode. The occurrence of the dysphoric manic episode was much unexpected, based on the clinical data found in the literature, which associate lamotrigine with a very low rate of switch into mania.*

Keywords: *Bipolar disorder, depression, therapy, lamotrigine.*

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**Correspondence:**

Elie Cheniaux

Rua Santa Clara, 50/1213 – Copacabana

Rio de Janeiro – RJ – Brazil

CEP 22041-010

Phone: + 55-21-2547-0670

E-mail: [echeniaux@globo.com](mailto:echeniaux@globo.com)