Obsessive Symptoms Associated with Lamotrigine use in a Patient with Bipolar II Disorder

Murat Kuloglu[1], Okan Ekinci[2], Elif Yilmaz[2], Ali Caykoylu[3]

ÖZET:
İkiuçlu II bozukluklu bir hastada lamotrijin kullanımı ile ilişkili obsesif belirtiler

Lamotrijinin ikiuçlu depresyonun akut tedavisi ve ikiuçlu bozukluk uzun dönem tedavisinde etkin olduğu bilinmektedir. Lamotrijin günümüzde de artan oranlarda ikiuçlu depresyon tedavisinde kullanılmaktadır. Lamotrijin kullanımının yol açtığı obsesyonel belirtilerle ilişkili literatür bilgisi kısıtlıdır. Biz bu yazıda almakta olduğu venlafaksin tedavisine lamotrijin eklenmesi ile başarılı bir şekilde tedavi edilmiş ancak lamotrijin doz arttırımı sonrasında obsesyonel belirtiler ortaya çıkmış ikiuçlu II bozukluk tanılı bir olguyu sunuyoruz.

Anahtar sözcükler: Lamotrijin, obsesyon, glutamat, ikiuçlu bozukluk

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ABSTRACT:
Obsessive symptoms associated with lamotrigine use in a patient with bipolar II disorder

Lamotrigine has been found to be efficacious in the acute management of bipolar depression and long-term management of bipolar disorder. Currently, it is increasingly used in the treatment of bipolar depression. Literature associated with obsessive symptoms related to lamotrigine treatment is limited. We report a case of bipolar II disorder that was successfully treated with pharmacological augmentation of lamotrigine plus venlafaxine and also subsequently experienced obsessive symptoms during treatment with lamotrigine.

Key words: Lamotrigine, obsession, glutamate, bipolar disorder

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[1]Associate Professor of Psychiatry, Firat University, Medical Faculty, Department of Psychiatry, Elazig-Turkey
[2] MD, [3]Associate Professor of Psychiatry, Atatürk Education and Research Hospital, Department of Psychiatry, Ankara-Turkey

Yazışma Adresi / *Address reprint requests to:* Dr. Murat Kuloğlu, Fırat Üniversitesi, Fırat Tıp Merkezi, Psikiyatri AD 23119 Elazığ-Turkey

Telefon / *Phone*: +90-424-233-3555

Faks / *Fax*: +90-424-238-8096

Elektronik posta adresi / *E-mail address:* kuloglum@yahoo.com

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INTRODUCTION

Lamotrigine, an anticonvulsant approved for the maintenance treatment of bipolar disorder in adults, has been proven to delay the time to occurrence of bipolar mood episodes and demonstrates particular efficacy in bipolar depression. Lamotrigine is currently being used to treat bipolar and unipolar mood disorders (1,2).

To our knowledge, there is limited literature available adressing obsessive symptoms possibly related to lamotrigine treatment in bipolar II patients (3,4). We report a female patient with bipolar II who developed obsessive symptoms that were associated with lamotrigine treatment and who subsequently experienced markedly improvement after dose reduction.

CASE REPORT

Mrs. C was a 31-year-old married woman with a high school education treated at our outpatient clinic. She had suffered from bipolar II disorder for the previous twelve years and had experienced four depressive episodes and two hypomanic episodes within that time. The first episode of her illness was a hypomanic episode at age 19. She had been treated with various antipsychotics (including risperidone and quetiapine), mood stabilizers (including lithium), and antidepressants (including fluoxetine, sertraline, venlafaxine) during this period. She had no personal history of substance abuse or previous psychiatric disorders, and no family history of mental illness.

Upon examination, she was found to suffer from severe pervasive sadness, anhedonia, insomnia, severe psychomotor retardation, feelings of worthlessness, distractibility, occasional passive suicidal ideation, and decreased energy, concentration, and self-esteem. She experienced these symptoms most of the time on most days and nearly every day during the month prior to admission. She was diagnosed with bipolar II disorder, depressive episode based on the diagnostic criteria of DSM-IV-TR (5). This was fifth depressive episode of her ilness. Initially, her 17-item Hamilton Depression Rating

Scale (HAM-D) (6) total score was 33.

At admission, the patient's physical, neurological, and laboratory examinations, showed normal findings. Although she had been regularly maintained on a treatment regimen (included venlafaxine XR 225 mg/day) for two months, her depressive symptoms continued. Subsequently, oral lamotrigine at a dose of 25 mg/day was added to the treatment regimen for the depressive episode, and the dose was gradually increased to 100 mg/day. However, two weeks after lamotrigine dose was increased to 100 mg/day, there was minimal clinical improvement in her depressive symptoms. Her HAM-D total score was 27. Therefore, lamotrigine dose was gradually increased to 150 mg/day. Seven days after lamotrigine dose was increased to 150 mg/day, her depressive symptoms significantly improved. Her HAM-D total score decreased to 5.

However, approximately ten days after the lamotrigine was increased to 150 mg/day, the patient experienced a new onset of intrusive and repetitive phrases without compulsion during the remission phase of her depression. She had not experienced any obsessive symptoms until that time. Some phrases began to intrusively repeat in her mind, such as “I had been expelled from various communities by other people” and another one “My friends had been behaved to me badly”. These phrases were time consuming (taking more than 4 hours per day) and were subjectively described as impairing her social interactions and functioning at work. Although she acknowledged that the phrases were irrational and meaningless she was not able to suppress them. She scored 14 of 20 on the obsession subscale of Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) (7). During the time she experienced emergence of obsessions there were not any symptoms suggestive of either a mixed episode including racing thoughts, insomnia, agitation and irritability or a hypomanic state. Subsequently, we decided to reduce lamotrigine dose because we believed that there is a possible association between the increase in lamotrigine dose to 150 mg/day and intrusive phrases. Thus, lamotrigine dose was gradually reduced to 50 mg/day. Only by the reduction of the lamotrigine dose, the intensity and frequency of the obsessive symptoms significantly diminished in one week. Eight days after reducing of the lamotrigine dose, the patient reported that the intrusive phrases had completely resolved. Her Y-BOCS obsession subscore was dramatically decreased from 14 to 2. At this time, she was on the remission phase of her depression. During the follow-up period, she did not report any obsessive symptoms with the same treatment regimen including lamotrigine 50 mg/day and venlafaxine 225 mg/day. In addition, the patient continued this combination regimen without recurrence of depression or emergence of hypomania or adverse effects for three months.

DISCUSSION

Lamotrigine is a phenyltriazine-derived anticonvulsant that stabilizes neuronal membranes and attenuates cortical glutamate release. It does have inhibitory effects on voltage-sensitive sodium channels and modulating effects have been noted on calcium and potassium channels (8). In addition, lamotrigine dose-dependently decreases extracellular serotonin and dopamine in rats, which could explain its effectiveness in preventing relapse of depression in bipolar disorder (9).

There is now a large body of evidence regarding the serotonergic basis of obsessive- compulsive symptoms. Recent functional, structural, and spectroscopic brain imaging data also suggests glutamatergic dysfunction in the cortico-striatal-pallido-thalamo-cortical tract (CSTC) dysfunction in obsessive compulsive disorder (OCD) (10,11). Therefore, the alteration in glutamate concentrations may contribute to the appearance of obsessionality with use of lamotrigine. Also, evidence indicates that OCD co-occurs with bipolar disorder, especially bipolar II, at a higher rate than in the general population. It has been suggested that bipolar II disorder population is more vulnerable to the expression of obsessionality (3,12). Moreover, abnormal glutamate levels are already known to exist within the dorsolateral prefrontal cortex in bipolar patients (13). So, it is possible to suggest that our patient may already have an intrinsic glutamate abnormality in her CSTC circuitry and may be particularly susceptible to the actions of lamotrigine upon the glutamatergic system. In addition, it has been suggested that obsessive-compulsive symptoms are associated with increased dopaminergic transmission (14). The inhibition of the excitatory neurotransmitter glutamate by lamotrigine may alter striatal dopamine uptake (8). This alteration may be another contributing

factor to emergence of obsessive symptoms in the present case.

As indicated by Kemp et al. (3), the complete remission of obsessive symptoms could be achieved not only by the cessation of drug but also by the dose reduction, like the present case. In addition, Kemp, et al. (3) emphasized that the emergence of intrusive phrases generally had first appeared when doses of lamotrigine >200 mg/day were prescribed. Subsequently, they suggested that high-dose treatment may also play a role in the appearance of the intrusive phrases. Our case indicates that obsessional symptoms associated with lamotrigine treatment could also occur at the lower doses of this agent. On the other hand, it is important to note that there are also literature data available on the adjunctive use of low dose lamotrigine in the treatment of OCD (15,16).

CONCLUSION

This report provides evidence that lamotrigine could induce obsessive symptoms in some patients, especially bipolar II, and suggests a dose-response relationship between lamotrigine and obsessive symptoms. However, it is unclear why lamotrigine induces obsessions in some patients. Further studies are necessary to enlighten the emergence of obsessions in the bipolar illness following treatment with lamotrigine and to investigate a possible dose-response relationship between obsessive symptoms and lamotrigine.

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