

Manic Attack Possibly Triggered by Sulbutiamine: Case Report

Muhtemelen Sulbutiamin ile Tetiklenen Bir Manik Atak Olgusu

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ABSTRACT Sulbutiamine is a precursor of thiamine that crosses the blood-brain barrier. The modulatory effects on both dopaminergic and glutamatergic transmissions within the prefrontal cortex could play a pivotal role in the therapeutic action of sulbutiamine. Sulbutiamine is currently used for the treatment of fatigue, exhaustion and asthenia in physical and psychiatric disorders; however, it does not have any psycho-stimulant properties. While sulbutiamine has no anti-depressive effect, it exhibits several psychotropic effects such as a decrease in psycho-behavioural inhibition occurring in major depressive disorder. In this report, we describe a possible case of sulbutiamine-triggered manic attack in a patient with major depressive disorder, who later developed bipolar I disorder with spontaneous manic episodes. To our knowledge, this is the first possible case of sulbutiamine-triggered manic attack at the proper therapeutic dosage of sulbutiamine in a major depressive patient.

Key Words: Sulbutiamine; bipolar disorder

ÖZET Sulbutiamin, tiaminin kan-beyin bariyerini geçen bir öncülüdür. Etki mekanizmasında prefrontal kortekste dopaminergik ve glutamaterjik iletiler üzerinde düzenleyici etkileri, muhtemelen önemli rol almaktadır. Sulbutiamin günümüzde fiziksel ve psikiyatrik hastalıklardaki yorgunluk, bitkinlik ve halsizliğin tedavisinde kullanılmaktadır. Buna karşın, hiçbir psiko-uyarıcı etkisi bulunmamaktadır. Sulbutiamin antidepresan etkiye sahip değildir, ancak majör depresif bozuklukta meydana gelen günlük aktivitelere karşı ilgi kaybı gibi psikososyal davranışlarda azalma gibi çeşitli psikotrofik etkiler sergilemektedir. Bu çalışmada, majör depresif bozukluğu bulunan bir hastada muhtemelen sulbutiamin tarafından tetiklenen manik atak olgusunu tanımladık. Bildiğimiz kadarıyla, bu vaka, uygun tedavi dozunda kullanılmasına rağmen sulbutiaminin majör depresif bir hastada tetiklediği ilk manik atak olgusudur.

Anahtar Kelimeler: Sulbutiamin; bipolar bozukluk

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Sulbutiamine is a hydrophobic molecule that easily crosses the blood-brain barrier and increases thiamine and thiamine phosphate esters in the brain.^{1,2} It does not have psycho-stimulant properties and is currently used for the treatment of somatic and psychic inhibitions. Sulbutiamine is not an antidepressant. It helps with psycho-motor inhibition during episodes of major depressive disorder and facilitates rehabilitation of patients in their social, professional, and family life functioning.³ Moreover, it improves performance in behavioural models of inhibition (induced by an aversive situation) such as “learned helplessness” and “forced swimming

tests".⁴ The changes in density of kainate receptors in the cortex after sulbutiamine injection lead to suggest that sulbutiamine and/or its metabolites may modulate the cortical glutamatergic transmission. Changed on glutamatergic transmission could initiate the modulation of dopaminergic cortical transmission. These interactions between dopaminergic and glutamatergic transmissions could play a pivotal role in the therapeutic action of sulbutiamine. These data strongly support recent findings that demonstrate improvement in behavioural, cognitive, attentional and functional disorders in schizophrenic, alcoholic and depressed patients.⁴

In this case, we report a possibly sulbutiamine-triggered manic attack in a patient with history of major depressive disorder.

CASE REPORT

Mrs. H, a 61-year-old married housewife with a history of one major depressive episode, was admitted for psychomotor agitation, decreased sleep, increased talkativeness and psychomotor activity. She was delusional and had an elated mood. She claimed that she was speaking with her dead parents. In her past psychiatric history, Mrs. H. had a major depressive episode three years before. She was treated with sertraline 50 mg/day for two years. As she continued to have some residual symptoms, her treatment was switched to venlafaxine 75 mg/day, which lasted seven months. Venlafaxine treatment was discontinued abruptly and sulbutiamine regimen was started by a general practitioner for asthenia 17 days prior to her presentation to our clinic with symptoms of a manic episode. She had been prescribed sulbutiamine 200 mg/day, 7 days earlier, sulbutiamine dose was increased to 400 mg/day because of no response to the treatment. Three days after the increased dose of sulbutiamine, psychomotor agitation and delusions have started. She became more talkative and developed inflated self esteem, decreased need for sleep, flight of ideas, distractibility, increased goal directed activity, and elevated and irritable mood. In psychiatric examination, she met criteria for manic episode according to DSM-IV⁵ criteria. Her Cli-

nical Global Impression for Illness score (CGI-I)⁶ was 6 and Young Mania Rating Scale (YMRS)⁷ was 29. The informed consent was obtained from the patient.

Results of a neurological and physical examinations, and laboratory tests were within the normal limits and she did not have any other medical disorders. Her vital signs were within the normal ranges. She did not have any history of substance abuse or dependence. Since routine work up studies were normal, no imaging studies were performed. The clinical presentation of patient was a classical manic episode, and there was no confusion, change in consciousness, or vital sign abnormalities pointing a possible delirium or cognitive disorder.

Family history of the patient was positive for bipolar disorder in her cousin, but she, herself did not have any history of manic or hypomanic episodes or psychotic disorders previously. Before this manic episode, she was taking only sulbutiamine without any other concomitant medications. After the diagnosis, sulbutiamine was discontinued and risperidone 4 mg/day was started. After two weeks on this treatment, pressured speech, elevated mood, and psychomotor agitation improved. Her CGI and YMRS scores decreased to 3 and 9, respectively. Low dose risperidone was continued (2 mg/day) and the patient's manic symptoms resolved completely within six weeks. Six months after her first manic episode, she stopped her medication by herself and a spontaneous manic attack occurred. She was diagnosed with bipolar I disorder.

DISCUSSION

Some psychoactive substances and medications can destabilize mood (e.g. alcohol and mefloquine-induced mania).^{8,9} In our case, the patient developed manic symptoms following a short course of sulbutiamine administration at the proper therapeutic dosage of 400 mg/day. An overdose of sulbutiamine (2000 mg/day) that triggered manic attack in a patient with a previous bipolar history was reported before.¹⁰

Our case had no history of manic/hypomanic but depressive episode previously treated with an

antidepressant. The presentation of symptoms after increasing the dose of sulbutiamine and absence of a manic switch with previous antidepressants pointed out a possible sulbutiamine induced manic attack. Venlafaxine treatment was discontinued at once. In addition, rare cases of manic episodes induced by antidepressant discontinuation have been reported in the literature. Those episodes are usually brief and self limited, and start within two weeks of antidepressant discontinuation.¹¹ Therefore, the severity of the presentation may suggest a reason other than a withdrawal syndrome. It took six weeks for the patient's manic episode to get in full remission with risperidone treatment. This does not rule out spontaneous or antidepressant discontinuation related manic episode.

She had been on venlafaxine for seven months without any adverse events. As she had a spontaneous manic episode six months after her drug induced first manic episode, she was diagnosed with bipolar I disorder and managed accordingly.

Although there is a significant variation among studies, the risk of antidepressant-induced

mania has been estimated at 20-40% in adult bipolar populations and less than 10% in unipolar depression.¹²

Possible mechanism of sulbutiamine triggered mania is not known. It might be idiosyncratic or related to psychoactive effects of sulbutiamine.

The authors postulate that sulbutiamine might exert a modulatory effect on glutaminergic and dopaminergic transmission in the prefrontal cortex. This could play a role in the psychoactive effect of sulbutiamine.⁴ It should be noted that manic episode did not occur during venlafaxine and sertraline treatment. Since the patient did not switch to mania under antidepressant treatments, sulbutiamine might have led to mania in a way other than known antidepressants mechanisms. Especially glutaminergic pathway etiology for switch must be kept in mind.

Clinicians should consider possibility of sulbutiamine triggering mania particularly in patients with history of bipolar disorder and inpatients who are at risk for bipolarity e.g. with positive family history of bipolar disorder.

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