

# Topiramate precipitating a manic episode in a bipolar patient comorbid with binge eating disorder

## A case report

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### Abstract

**Rationale:** Topiramate is a novel antiepileptic drug that is used as an adjunctive in the treatment of partial and secondary generalized seizures. In recent years, psychiatrists have paid more attention to topiramate as a mood stabilizer and as an agent for treating eating disorders, especially in binge eating disorder (BED) and bulimia nervosa.

**Patient concerns and diagnoses:** Herein, we report a case of topiramate precipitating a manic episode in a bipolar patient comorbid with BED, who complained of emotional instability and binge-eating behaviors.

**Diagnoses:** In this patient, acute manic episode was induced by topiramate treatment at a daily dose of 75 mg for three days.

**Interventions:** The dose of topiramate was decreased to 25 mg per day promptly, and the patient gradually became calm but the BED symptoms recurred, then the dose of topiramate was increased to 50 mg per day again. Meanwhile, the dosage of quetiapine was escalated up to 500 mg per night to stabilize her mood.

**Outcomes:** With a combination of quetiapine 500 mg per night and topiramate 50 mg per day, the emotion and eating problems of this patient concurrently improved.

**Lessons:** These findings indicated that patients with a history of bipolar disorder and comorbid BED have a tendency to develop manic episode when taking topiramate. Careful monitoring of mood alterations after topiramate supplement to mood stabilizers is necessary in this population.

**Abbreviations:** AMPA =  $\alpha$ -amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid, BD = bipolar disorder, BED = binge eating disorder, BN = bulimia nervosa, CYP = cytochrome oxidase P450, ED = eating disorder, GABA = gamma-amino butyric acid, YMRS = Young Manic Rating Scale.

**Keywords:** binge eating disorder, bipolar disorder, mania, topiramate

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## 1. Introduction

Topiramate is a novel antiepileptic drug, which is initially used as an adjunctive in the treatment of partial and secondary generalized seizures. In recent years, psychiatrists have showed more interest in topiramate as an adjuvant to treat eating disorders (EDs), such as bulimia nervosa (BN) and binge eating disorder (BED).<sup>[1]</sup> The underlying mechanisms of topiramate in treating BED is possibly restricting eating behaviors through suppressing appetite, inducing weight loss by stimulation of energy expenditure, and reduction of energy intake.<sup>[2]</sup> In addition, topiramate treatment is also associated with reductions of other impulsive or addictive behaviors, such as alcohol and cocaine use.<sup>[3,4]</sup>

To date, there was no firm conclusion on treatment efficacy of topiramate for bipolar disorder (BD).<sup>[5]</sup> BD can often comorbid with EDs, and the BED cases were the most common type of EDs among the bipolar population.<sup>[6,7]</sup> As reported, 9% of the EDs subjects had suffered from hypomania or major depressive disorder.<sup>[8]</sup> In another study, 15% of the subjects were found to have type II BD and none was found to have type I BD.<sup>[9]</sup> Pharmacological management of both disorders includes mood

stabilizers, atypical antipsychotics, antidepressants, and anti-convulsants. Topiramate, as an anticonvulsant, seems to have a role in managing patients with both BD and BED. However, in patients with a history of seizures or prior psychotic history, topiramate may induce manic episodes in some cases.<sup>[10,11]</sup> In this case study, we reported that topiramate induced a manic episode in the course during BD and BED treatment.

## 2. Case presentation

A 22-year-old female was admitted to our hospital, because of her recurrent mood swings for over 9 months. Initially, this patient spontaneously became abnormally happy, talkative, energetic, and irritable for three to five days. However, this experience had little influence on her daily life and she did not take it seriously. 3 months ago before admission, her emotion went down and she manifested loss of interest, irritability, difficulty in falling asleep, and early awakening. Meanwhile, this patient became inattention and poor memory, and her scholar performance in school began to fall gradually. Of note, the patient had eating problems and sometimes would eat a lot within a few hours. This uncontrollable eating behavior occurred about three or four times each week, and had last for 3 months. She had suicidal thoughts and attempts prior to hospitalization.

On admission, physical and neurologic examinations did not identify any abnormalities. The height of this patient was 150 cm and the weight was 51 kg, and the BMI was 22.67 kg m<sup>-2</sup>. She had no developmental problems, no history of alcohol consumption, smoking, or illegal substance use. No family history of psychiatric illnesses was reported. Laboratory examinations such as routine blood tests, biochemical indexes, infectious markers, and thyroid hormones were all in the normal references. Electroencephalogram and cranial magnetic resonance imaging were also normal. She was diagnosed with bipolar II disorder, depressive episode, and BED, according to the Diagnostic and Statistical Manual of Mental Disorders, the Fifth Edition.<sup>[12]</sup>

She was then prescribed with quetiapine, which was gradually increased to a dose of 300 mg per night in the first week. Her emotion improved and irritability disappeared. However, the BED symptoms still existed in the first 10 days. Accordingly, she was prescribed with topiramate 25 mg per day for four days, and the dose of topiramate was increased to 50 mg for four days, and 75 mg per day eventually. At the meantime, the dose of quetiapine was kept at 300 mg per night and the emotion of our patient was stable. The patient's eating problems disappeared and no impulsive eating behaviors were observed again from then onwards. Three days after taking topiramate 75 mg per day, however, the patient appeared to be excited, talkative, active, and energetic. These symptoms persisted for four days and she scored 30 out of 44 points on the Young Manic Rating Scale. A mania episode was considered and topiramate was thought to be the culprit. Therefore, the dose of topiramate was decreased to 25 mg per day promptly, and the patient gradually became calm in the next 2 days. However, the BED symptoms recurred and the dose of topiramate was again increased to 50 mg per day. Meanwhile, the dosage of quetiapine was escalated up to 500 mg per night to stabilize her mood. Finally, with a combination of quetiapine (500 mg per night) and topiramate (50 mg per day), the emotion and eating problems of this patient concurrently improved. Her condition remained stable at follow-ups four months after hospital discharge.

This work was approved by the Hospital Ethical Committee (Reference Number: 2018–1061), and written informed consent was given by the patient and her guardian, who approved the publication of the case details.

## 3. Discussion

Topiramate has been demonstrated to cause adverse drug reactions in the central nervous system, such as headache, dizziness, cognitive impairments, behavioral changes, and fatigue.<sup>[13,14]</sup> In our present case, the patient who had comorbid BD and BED suffered from a manic episode possibly elicited by topiramate.

Previous studies have demonstrated a high comorbidity of BDs and EDs, especially of BN and BED. A recent genome-wide association study on BD with binge-eating behavior has revealed potential genetic etiology.<sup>[15]</sup> Bipolar patients with binge-eating behavior are more likely to present higher levels of anxiety and emotional reactivity.<sup>[16]</sup> As for treatment, a combination of lithium and topiramate is indicated by previous studies for both disorders.<sup>[17]</sup> In addition, case reports also showed lamotrigine or electroconvulsive therapy may also be beneficial for concomitant BD and BED.<sup>[18,19]</sup> In our patient, we chose a combination of quetiapine and topiramate to manage both conditions. As an antiepileptic drug, topiramate exerts its biochemical functions in the brain by multiple pathways, such as blocking sodium channels and L-type calcium channels, potentiating gamma-amino butyric acid (GABA), antagonizing  $\alpha$ -amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA)/kainate receptors, and inhibiting carbonic anhydrase isoenzymes. Topiramate has also been hypothesized to induce psychosis due to its anti-glutamatergic property in the nucleus accumbens and prefrontal cortex.<sup>[20]</sup> In addition, topiramate has been reported to cause mood swings in 1%–3% of the subjects.<sup>[10]</sup> Topiramate may induce manic episodes in patients with a history of seizures or prior psychiatric illnesses.<sup>[10,11]</sup> In the case reported by Jochum,<sup>[10]</sup> an alteration in AMPA neurotransmission was considered to be the cause of topiramate-associated manic episode.

The mood stabilizer used in our patient was quetiapine. Quetiapine is one of the first-line drugs recommended for the treatment of BD in either the acute phase or in remission.<sup>[21,22]</sup> The possible cause of manic episode in our case could be the drug interaction between topiramate and quetiapine. It is known that the enzyme inducers can increase the elimination of one drug, leading to a lower plasma concentration of this drug. Topiramate itself is a weak inhibitor of cytochrome oxidase P450 (CYP) 2C19, but an inducer of CYP3A4 as well. Consequently, topiramate can promote the clearance of quetiapine by activating CYP3A4 enzyme system, and lower the plasma concentration of quetiapine. The falling of plasma concentration of quetiapine may then lead to mood fluctuations. In our patient, the manic symptoms occurred when the dose of topiramate was increased to 75 mg per day, and recovered after the dose was decreased. Given the drug interactions between quetiapine and topiramate, the dose of quetiapine was increased to 500 mg per night. The emotion and eating behaviors kept normal during follow-ups.

In conclusion, this case report is descriptive and has some limitations, such as lack of controls, open-label design, and no verifications in larger samples. However, this study is still indicative that topiramate supplement in bipolar patients with binge-eating behaviors may precipitate manic episodes, especially

in combination with quetiapine treatment. Careful considerations are required to manage both symptoms to avoid potential side effects and harbor more benefits.

### Author contributions

**Funding acquisition:** Jing Lu.

**Writing – original draft:** Jinfeng Duan, Jianbo Lai, Dandan Wang, Weihua Zhou, Manli Huang.

**Writing – review & editing:** Jinfeng Duan, Shaohua Hu, Yi Xu, Jing Lu.

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