

Topiramate precipitating mania in bipolar disorder

Sir,

Topiramate is a novel antiepileptic drug (AED) as an adjunctive in the treatment of partial and secondarily generalized seizures. Initially, psychiatrists showed an interest in topiramate as a mood stabilizer but its efficacy in bipolar disorder was found to be negative across studies.^[1] Neuropsychiatric adverse effects in clinical trials though were not significantly different from placebos; concerns remain about its use, particularly in predisposed patients. The incidence of confusion, depression, anxiety, delusions, perceptual disturbances, and cognitive impairment with topiramate is rare but the risk is high in preexisting psychiatric conditions.^[2] Patients with history of prior psychotic or depressive symptoms had a tendency to develop the same type of mood disorder when put on topiramate. We present a case of a bipolar patient prescribed on topiramate who presented with an acute manic relapse.

A 26-year-old female diagnosed with bipolar affective disorder, in remission for 1 year on sodium valproate 700 mg/day consulted a neurologist for headache and was prescribed topiramate 25 mg/day. Considering improvement in frequency and severity of the headache, the dose of topiramate was hiked to 37.5 mg/day in 1 month. Within 2 weeks of hiking the dose of topiramate, the patient was brought to the psychiatrist with complaints of increased talk, over activity, reduced need for sleep, and grandiose ideas. She was diagnosed with mania with psychotic symptoms and the dose of sodium valproate was hiked to 800 mg/day and olanzapine 5 mg/day was also added. Considering no improvement in 3 days, the dose of sodium valproate was hiked gradually up to 1,200 mg/day, Olanzapine was hiked to 10 mg/day and chlorpromazine was added 200 mg/day. Later topiramate was stopped as the symptoms persisted, leading to resolution of the symptoms within 1 week. Currently, the patient remains stable on sodium valproate 1,200 mg/day and olanzapine 2.5 mg/day.

The antiepileptic topiramate acts by blocking sodium channels, potentiating gamma-aminobutyric acid (GABA), and antagonizing alfa-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptors of glutamate. Topiramate has been hypothesized to induce psychosis as a result of its antiglutamatergic properties in nucleus accumbens and prefrontal cortex.^[3] Topiramate is known to cause mood swings in 1-3% of the subjects. This case is illustrative of a potentially severe side effect of topiramate by precipitating mania possibly due to alteration in amino acid neurotransmission.^[3]

Another possible cause of manic relapse in our case could be the drug interaction, though minimal between topiramate and valproate. It is known that the simultaneous use of topiramate and valproate increases the plasma levels of the first by 15% and

on the other hand, topiramate increases valproate clearance, thus reducing its plasma levels.^[4] The failure of valproate might have led to the current manic episode. Thus, the etiological role in relapse though could not be exclusively attributed to neurochemical mechanisms of topiramate. We need systematic data on the use of topiramate in bipolar disorder to ascertain the risk.

Topiramate is finding new indications in the management of numerous medical conditions including neuropsychiatric disorders. Apart from epilepsy, it is now widely used in migraine, cluster headache, obesity, substance addiction, bulimia nervosa, and essential tremors. Most of these are known to be highly comorbid with bipolar disorder. It is also used for reducing weight gain associated with antipsychotics^[5] in patients with schizophrenia and bipolar disorder. Thus, the clinician should be aware of this rarest side effect so as to not confuse it with the emergence of new episode due to ineffectiveness of mood stabilizers in the event of relapse. Utmost caution and vigilance for an affective episode is required while starting topiramate. Evaluation of psychiatric history during prescription would help in determining vulnerable patients.

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Conflicts of interest

There are no conflicts of interest.

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