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Case Report

Acute psychosis induced by topiramate

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ABSTRACT

Topiramate (TPM) is a new potent antiepileptic drug (AED) used as add-on therapy for generalized and partial seizures that are resistant to the other AEDs; or as a mood stabilizer, and for reducing weight gain associated with olanzapine and clozapine in patients with bipolar disorder or schizophrenia. However, there is a higher risk of psychosis with TPM in patients with a past history of psychiatric disorder. This case report highlights emergence of psychosis that was related to TPM which resolved on discontinuation.

Keywords: Topiramate, Mania Rating Scale, Brief Psychiatric Rating Scale, Drug–drug interaction, CYP450

INTRODUCTION

Topiramate (TPM) is a new potent antiepileptic drug (AED) with antiepileptic activity mediated by multiple mechanisms, such as blockade of voltage-dependent sodium channels and glutamatergic mechanisms, and potentiation of gaba amino-buteric acid (GABAergic) mechanisms.[1] It is used as an add-on therapy for generalized and partial seizures that are resistant to the other AEDs and as a mood stabilizer for patients with bipolar disorders[2] and schizophrenia.[3,4] The new anticonvulsant TPM has not yet been studied systematically as primarily a weight loss agent, but it has been associated with decrease in appetite and weight loss in patients with epilepsy and bipolar disorder.[1,5] However, the risk of psychiatric adverse effects related to TPM may be greater in patients with a past history of psychiatric events and there have been case reports of psychosis such as visual and auditory hallucinations that were temporally related to TPM therapy.[6] The purpose of this paper is to report a rare case which presented with psychosis after the use of TPM.

CASE REPORT

Mrs. X aged 30 years, postgraduate (MA), married female, and a mother of two children, reported in the outdoor patient unit, Department of Psychiatry, Government Medical College, Rajindra Hospital, Patiala with the complaints of over-talkativeness, over-familiarity, over-religiosity, euphoric in mood, decreased need for sleep, increased appetite and suspiciousness that people pass comments on

her or they look upon her in strange way and with violent outbursts putting her in great trouble with others for the last 1 month. There were two past episodes of mania and one episode of depression during the last 5 years. There was significant social and occupational work impairment and these symptoms were not due to any other medical, substance or psychiatric illness. The last episode of depression occurred 2 years ago which was precipitated by untimely death of her father, aged 65 years who died of cardiovascular event. She took lamotrigine 200 mg/day for 8 months under supervision of the psychiatrist and recovered from an episode of depression. She has two children aged 5 and 3, both males and had a first episode of high on mood when she was 25 years, after the birth of her eldest son. These symptoms occurred within a month of her delivery and lasted for 3 months which resolved on medication. On mental status examination, she was conscious, distractible, though oriented to time, place, and person. Eye to eye contact was made and rapport established with difficulty, mood was euphoric; affect appropriate to the mood content, with flight of ideas, delusion of grandiosity "identity" and fleeting delusion of reference and second person "auditory hallucinations". Judgment was poor, insight to the illness, and reality contact was broken. According to the International Classification of Disease: Clinical Descriptions and Diagnostic Guidelines (ICD-10), she was diagnosed a case of F 31.21 bipolar affective disorder, current episode mania with mood-incongruent psychotic symptoms. She was started with divalproex sodium 1500 mg/day, olanzapine 10 mg/day and lorezepam 2 mg/day at bed time. Her baseline Mania Rating Scale (MRS) score 43, Brief Psychiatric Rating Scale (BPRS) score 79, Clinical Global Impression (CGI) score 6, and baseline weight was 62 kg. After 4 weeks, the score on MRS, BPRS, and CGI was 21, 48, and 4, respectively; indicating response (50% reduction). The gain in the weight after 4 weeks was 5 kg (i.e., 67 kg) with CGI-efficacy index 0.75 indicating metabolic side-effects which outweigh therapeutic response. The patient reported voracious appetite and weight gain which could be attributed to either drug olanzapine or divalproex sodium. The laboratory investigations for complete blood count, urine test, fasting blood sugar, liver function test, renal function test, thyroid function test, electrocardiogram, and ultrasound for abdomen were normal. The possibility of divalproex sodium causing increase in appetite was unlikely as the liver function test was normal. Olanzapine could have been the offending drug in causing weight gain therefore TPM 25 mg/day was started, but within 24 hrs. of the drug (TPM) there was re-emergence of symptoms of delusion of reference and second person "auditory hallucination". The MRS, BPRS score was 37, 77 and Global CGI score indicating much worsening, with CGI-efficacy index 0.25. TPM was stopped and after 24 hrs. of abstinence, the re-emerged symptoms of psychosis abated with the MRS, BPRS score returned to 27, 47, and Global CGI score showing much improvement. Thus, the diagnosis of TPM-induced psychosis was made.

DISCUSSION

TPM-related cognitive decline is generally mild to moderate in severity. The use of gradual dose titration and relatively low (i.e., <200 mg/day) final doses may reduce the incidence of psychiatric and cognitive related events. Symptoms of psychosis have been seen in some patients receiving TPM, but it is not clear whether the incidence is greater than that expected in populations with severe epilepsy. A past psychiatric history was a predictor of both cognitive and psychiatric adverse events.[6] There have been case reports of psychosis that were clearly temporally related to TPM therapy that resolved when TPM therapy was discontinued.[7-9] In the case, according to ICD-10, patient was diagnosed as bipolar affective disorder, current episode mania with psychosis. She was given mood stabilizer divalproex sodium and gradually titrated up to 1500 mg/day with an atypical antipsychotic olanzapine 5-10 mg/day. There are few reports which highlight increased appetite and resulted weight gain with olanzapine.[10] In this case, although the symptoms of psychosis remitted with olanzapine yet, it resulted in increased appetite and weight gain. As TPM has been associated with decrease in appetite and weight loss in patients of bipolar disorder,[5] so she was started with TPM 25 mg/day on 4th week but within 24 hrs there was re-emergence of the symptoms of psychosis which abated when the drug was stopped within the next 24 hrs. It highlights that TPM having elimination plasma half-life *t* ½ of 19-25 hrs. may be the reason for early remission of treatment emergent psychosis when the drug (TPM) was stopped. The possibility of drug interaction with olanzapine is less likely as drug interaction of risperidone is the only documented evidence with TPM.[11] In the case, olanzapine a 1A2 substrate was given, which is metabolized by CYP 2D6 enzyme and phase II glucuronidation[12] whereas TPM is a 3A4 inducer and inhibitor of 2C19.[13] The symptoms of psychosis re-emerged after the start of TPM highlight the pharmacodynamic or intrinsic properties of TPM to induce psychosis in patients having underline mental illness[6] which abates after stopping. Although, these preliminary results are encouraging yet, to understand the rationale of controlling metabolic side-effects due to atypical anti-psychotics; further prospective, controlled, and adequately powered statistical studies are needed to guide evidence-based clinical practice.

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