Topiramate-induced psychosis: report of two cases

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Topiramate-induced psychosis: report of two cases

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Topiramate (TPM) has widespread use as an anticonvulsant, and recent studies highlighted its neurostabilising activities at multiple receptors and ion channels [1]. TPM has also been used as a mood stabiliser, an augmentation agent in bipolar disorders, and in the management of both selective serotonin re-uptake inhibitors and neuroleptic-induced weight gain in anxiety disorder patients [1,2]. On the other hand, the use of TPM has limitations with 8 – 26% of patients enrolled in clinical trials discontinuing treatment due to side effects [2,3]. The most common adverse events reported include somnolence, nausea, anorexia, weight loss, paresthesias, psychomotor slowing, dizziness, renal calculi, emotional liability, anxiety and behavioural disturbances [2-4].

We report two cases TPM induced psychosis in both epileptic and nonepileptic patients controlled after drug withdrawal.

The first is a 23-year-old male with mental retardation and idiopathic epilepsy treated initially with carbamazepine 200 mg t.i.d and olanzapine 5 mg t.i.d. After 6 months on this regimen he developed significant weight gain and carbamazepine was discontinued with introduction of TPM (initially 50 mg qd followed by weekly 50 mg daily dosage increases). When the total daily dosage reached 300 mg, the patient developed paranoid persecutory ideation, recurrent death thoughts, repetitive manipulation of his own genitalia, severe aggressive behaviour and echolalia. All symptoms gradually disappeared after TPM was discontinued with concomitant increase in olanzapine dosage (total 20 mg/day).

The second is the case of a 17-year-old male with mental retardation of unknown cause, chronic morbid obesity (body mass index 40.2 kg/m²) and anxiety disorder treated with citalopram 40 mg qd and clonazepam 2 mg b.i.d. After 4 months he started with symptoms of compulsive eating behaviour and TPM was slowly introduced and titrated up to a dosage of 500 mg/day (started at 50 mg qd with 50 mg daily dosage increase every 5 days), which controlled symptoms. After three weeks in this regimen, the patient presented with visual hallucinations, persecutory paranoid ideation, worsening of anxiety, and he was constantly afraid to fall asleep during the day or night. TPM and citalopram were reduced to 300 and 20 mg/day, respectively. After 2 weeks his psychotic behaviour improved, but paranoid ideation intermittently recurred. TPM was then discontinued and a week later he was free of symptoms.

Available data regarding TPM-induced psychosis come from series assessing retrospectively the occurrence of neuropsychiatric adverse effects of TPM [4,5]. Frequencies ranged from 3.7 to 12% and most patients were epileptic also receiving other anticonvulsants. Risk factors identified include high starting dose, rapid titration, family history of psychiatric illnesses and epilepsy, personal history of febrile convulsions, psychiatric history, and presence of tonic-atonic seizures. Dosages at the time of symptoms onset ranged from 50 to 400 mg/day. The mechanisms underlying psychotic symptoms in these patients remain obscure. A GABAergic hypothesis with inhibition of the substantia nigra and overactivity of ascending dopaminergic pathways has been proposed, but remains speculative [5].
According to the experience of others presented in the literature and by the cases presented here, symptoms usually resolve with TPM discontinuation or dosage reduction, although neuroleptics have been used until remission and necessary dosage adjustments are completed [4,5]. Despite documentation of several significant side effects, TPM is still considered safe and effective with good tolerance and favourable pharmacokinetics if used with proper dose escalation and precise indications.

Bibliography


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