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Case Report

A Case of Psychosis Due to Topiramate Treatment: Review of the Literature

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Abstract

Topiramate is a wide spectral antiepileptic agent with multiple mechanism of action effective on epilepsy, migraine, pain syndromes, and several movement disorders. As well as the most common side-effects including nausea, weight loss, fatigue, psychomotor slowing, renal calculi and metabolic acidosis, we presented a relatively rare case of psychosis due to topiramate treatment, reviewed the literature.

Keywords: Topiramate; Side-Effects; Psychosis.

Introduction

Topiramate is a wide spectral antiepileptic agent which is found to be effective on partial and primary generalized tonic-clonic seizures, as well as tonic-atonic seizures associated with the Lennox-Gestaut syndrome (1-3). In addition to epilepsy, topiramate has shown to be effective in migraine, several pain syndromes, and movement disorders including restless leg syndrome, tics, and tremor (4, 5).

This broad range of efficacy in different diseases can be attributed to its multiple mechanisms of action such as voltage-gated calcium channel blockage to modulation of synaptic neurotransmission, voltage-gated sodium channel blockage, potentiation of the inhibitory γ-aminobutyric acid (GABA)-mediated neurotransmission through an interaction with the $GABA_A$ receptors, the inhibition of neuronal excitatory pathways through a selective action at the α-amino-3-hydroxy-5-methyl-4-isoxazole-propionic acid (AMPA) and kainate subtypes of glutamate receptors, weak inhibition of type II and type IV carbonic anhydrase (CA), and demonstrated a biphasic effect of topiramate on kainate-evoked currents as revealed by an initial inhibition of the kainate-evoked currents, followed by a delayed additional inhibitory effect (6, 7).

On the basis of these different mechanisms of action, the most common side effects of topiramate can be summarized as weight loss, heat intolerance, hypohydrosis, renal calculi, metabolic acidosis, and ophthalmologic effects. Moreover, somnolence, fatigue, headache, psychomotor slowing, confusion, impaired concentration and attention, speech and language problems with memory impairment are the most frequent central nervous system side-effects of the drug (8).

In contrast to a case revealing the positive effect of topiramate on psychotic symptoms such as agitation and hallucinations (9), we reported patient with epilepsy dealing with life-threatening psychotic changes in behavior due to topiramate treatment.

Case-Report

A 49-year old right-handed woman presented to the emergency room with partial onset convulsions in the right arm which are secondary generalized and accompanying loss of consciousness. The patient was hospitalized to the neurology clinic and she was seizure free after intravenous levetiracetam infusion. Upon regaining her consciousness, she had aggressive behaviors, agitations. She was yelling and swelling to her siblings. She had paranoid thoughts, and was attacking to her siblings with the thought to be harmed. Her psychiatric evaluation revealed acute psychosis and 25 miligrams of ketiapine twice daily was administered to the patient. Her siblings stated that she had diabetes under control with oral antidiabetic agents. She had the diagnosis of epilepsy since 14 years, and her seizures had partial onset with motor features which were gradually becoming generalized with loss of consciousness. She was treated with various AED since she got the diagnosis of epilepsy. However she was under topiramate treatment 100 milligram per oral twice daily since 2 years. Under topiramate treatment, she was experiencing secondary generalized seizures once a month and her behavioral changes began 1 month after the administration of the drug including aggressiveness, paranoid thoughts leading to attacks with knife, yelling and swellings. While these behavioral changes were only in the postictal phases of the episodes lasting 1 week in the first years of topiramate treatment, her siblings stated that these behavioral changes gradually increase in frequency spreading to the interictal phases and became permanent in the last year with extreme skepticism, excessive aggressiveness, agitations, anger explosions

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giving harm to her neighborhood. The patient experienced no epileptic event with levetiracetam and atypical antipsychotic treatment during her hospitalization. Her vital parameters were normal. Neurological examination of the patient was normal, except behavioral examination revealing psychosis. There were no abnormalities in routine blood tests and toxicology analysis of the patient. Cranial magnetic resonance imaging of the patient was also normal. Electroencephalographic evaluation of the patient was consistent with postictal phase. Acute psychotic symptoms were settled with antipsychotic treatment without any seizures.

Discussion

Topiramate is an AED with multiple mechanisms of action including blockage of voltage-gated sodium channels, antagonism of AMPA/cainate-glutamate receptors, weak carbonic anhydrase inhibition (7). The common adverse effects of topiramate can be summarized as metabolic acidosis, weight loss, nausea, diarrhea, difficulties in concentration and speech, psychomotor slowing (10). Due to its wide range of molecular action, it has been shown to be effective in a number of neuropsychiatric disorders (9). However, it is also well-known that it can cause cognitive deterioration, psychomotor slowing and abnormal thinking (11).

In addition, behavioral changes can be seen due to topiratame treatment including emotional lability, increased anxiety, and aggressive behavior (12). Psychotic symptoms which are relatively rare have also been reported with previous studies (12, 13). There has been suggestion that topiramate acts both directly and indirectly on the brain causing psychosis, and that seizure freedom for people who have epilepsy was associated with psychosis (14, 15). Kober and Gabbard described topiramate-induced psychosis in a case that was not epileptic where topiramate was used for mood stabilisation and weight loss for a patient with obsessive compulsive disorder (16).

However, the relationships between AEDs, epilepsy and psychosis are complex and still poorly understood (17). Thus, to assess the psychotropic effects of AEDs, further large-scale, prospective, randomized, double-blind; placebo-controlled studies that are properly designed to assess psychotropic effects studies are needed.

References

1. Biton V, Montouris GD, Ritter F, Riviello JJ, Reife R, et al. 1999 A randomized, placebo-controlled study of topiramate in primary generalized tonic-clonic seizures. TopiramateYTC Study Group. Neurology, 52(7): 1330-1337.

2. Sachdeo RC, Glauser TA, Ritter F, Reife R, Lim P, et al. 1999 A double-blind, randomized trial of topiramate in Lennox-Gastaut syndrome. Topiramate YL Study Group. Neurology, 52(9):1882-1887.

3. Elterman RD, Glauser TA, Wyllie E, Reife R, Wu SC, et al. 1999 A double-blind, randomized trial of topiramate as adjunctive therapy for partial-onset seizures in children.Topiramate YP Study Group. Neurology, 52(7):1338-1344.

4. Linde M, Mulleners WM, Chronicle EP, McCrory DC. 2013 Topiramate for the prophylaxis of episodic migraine in adults. Cochrane Database Syst Rev, 6.

5. Zesiewicz TA, Elble RJ, Louis ED, Gronseth GS, Ondo WG, et al. 2011 Evidence-based guideline update: treatment of essential tremor: report of the Quality Standards subcommittee of the American Academy of Neurology. Neurology, 77(19): 1752-1755.

6. Shank RP, Gardocki JF, Streeter AJ, Maryanoff BE. 2000 An overview of the preclinical aspects of topiramate: pharmacology, pharmacokinetics, and mechanism of action. Epilepsia, 41.

7. White HS. 2003 Mechanism of action of newer anticonvulsants. J Clin Psychiatry, 64 Suppl 8: 5-8.

8. French JA, Kanner AM, Bautista J, Abou-Khalil B, Browne T et al. 2004 Efficacy and tolerability of the new antiepileptic drugs II: treatment of refractory epilepsy: report of the Therapeutics and Technology Assessment Subcommittee and Quality Standards Subcommittee of the American Academy of Neurology and the American Epilepsy Society. Neurology, 62(8): 1261–1273.

9. Ochoa JG. 2014 Topiramate improves psychiatric symptoms in a patient with Lewy body dementia. Cogn Behav Neurol, 27(4): 222-223.

10. Gupta PP, Thacker AK, Haider J, Dhawan S, Pandey N, Pandey AK. 2014 Assessment of topiramate's efficacy and safety in epilepsy. J Neurosci Rural Pract, 5(2): 144-148.

11. Mula M. 2012 Topiramate and cognitive impairment: evidence and clinical implications. Ther Adv Drug Saf, 3(6): 279-289.

12. Weintraub D, Buchsbaum R, Resor Jr SR, Hirsch LJ. 2007 Psychiatric and behavioural side effects of the newer antiepileptic drugs in adults with epilepsy. Epilepsy Behav, 10(1): 105-110.

13. Mula M, Trimble MR, Lhatoo SD, Sander JW. 2003 Topiramate and psychiatric adverse events in patients with epilepsy. Epilepsia, 44: 659-693.

14. Mula M, Monaco F. 2009 Antiepileptic drugs and psychopathology of epilepsy: an update. Epileptic Disord, 11(1): 1–9.

15. Mula M, Trimble MR, Sander JW. 2007 Are psychiatric adverse events of antiepileptic drugs a unique entity? A study on topiramate and levetiracetam. Epilepsia, 48(12): 2322–2326.

16. Kober D, Gabbard GO. 2005 Topiramate-induced psychosis. Am J Psychiatry, 162(8): 1542.

17. Besag FM. 2001 Behavioural effects of new anticonvulsants. Drug Saf, 24 (7): 513-536.