

Psychotic symptoms due to topiramate

Objawy psychotyczne wywołane stosowaniem topiramatu

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Abstract

Topiramate is an antiepileptic drug prescribed in the treatment of numerous psychiatric disorders and in epilepsy. Topiramate exerts its antiepileptic effect through different mechanisms, such as by the blockage of sodium channels, increasing GABAergic neurotransmission, antagonizing excitatory amino acid receptors (glutamate) or blocking calcium channels. Its prescription in psychiatric diseases has increased in recent years and psychotic symptom development due to the usage of topiramate has been observed in some studies. Therefore, it is essential to evaluate the patient for psychotic symptoms while using topiramate. This article presents a case of a 37-year-old woman who developed depression, anxiety and auditory hallucinations during the treatment with 150 mg of topiramate. After stopping topiramate, 5 mg of olanzapine bid was started and the symptoms gradually decreased and finally disappeared.

Key words: auditory hallucinations, psychotic symptoms, topiramate

Streszczenie

Topiramat to lek przeciwdrgawkowy przepisywany w leczeniu wielu zaburzeń psychicznych i padaczce. Mechanizm działania przeciwdrgawkowego jest wielokierunkowy – np. lek ten blokuje kanały sodowe, stymuluje transmisję w układzie GABA-ergicznym, antagonizuje receptory dla pobudzających aminokwasów (glutaminian) oraz blokuje kanały wapniowe. Jakkolwiek w ostatnich latach topiramat przepisywany jest coraz częściej w leczeniu zaburzeń psychicznych, to jednak w kilku badaniach zgłaszano występowanie objawów psychotycznych w następstwie jego stosowania. Z tego względu szczególnie ważna jest ocena pacjentów stosujących ten lek pod kątem występowania objawów psychotycznych. Autorzy przedstawiają przypadek 37-letniej pacjentki, u której w związku z leczeniem z użyciem 150 mg topiramatu rozwinęły się depresja, zaburzenia lękowe i omamy słuchowe. Po odstawieniu topiramatu zalecono stosowanie 5 mg olanzapiny dwa razy dziennie. Objawy stopniowo zanikały, aż do całkowitego ustąpienia.

Słowa kluczowe: omamy słuchowe, objawy psychotyczne, topiramat

INTRODUCTION

Anticonvulsant drugs are being increasingly used in the treatment of psychiatric disorders. Topiramate, synthesised in 1979 and made available in England in 1995 for the first time, was licensed in 1996 by the U.S. Food and Drug Administration for adults and children aged 2–16 in the treatment of partial onset seizures or primary generalised tonic-clonic seizures. Antiepileptic drugs exert their antiepileptic effects through different mechanisms, such as by the blockage of sodium channels, increasing GABAergic neurotransmission, antagonizing excitatory amino acid receptors (glutamate) or blocking calcium channels. Topiramate combines the pharmacological profiles of carbamazepine and valproate. This creates a biological basis for a more comprehensive antiepileptic activity, and the drug can be useful in the treatment of bipolar disorder. In addition, it is suggested that glutamate alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionate (AMPA) receptor antagonism is another feature of topiramate which strengthens GABAergic transmission (Ortho-McNeil Pharmaceutical, Inc., 1999). It is proposed that this combined mechanism of action of topiramate may be effective in a variety of anxiety disorders. Moreover, the efficacy of topiramate in migraine prophylaxis has been shown in a consistent manner in four big studies. Topiramate is effective in migraine prevention, and it is among the first-line drugs for migraine treatment, along with beta-blockers and flunarizine. Its effective dose is between 25 and 100 mg/day (Evers, 2008; Evers *et al.*, 2009; Taylor, 2008). It has been shown in several studies that the direct or indirect use of topiramate may lead to the exacerbation or development of psychotic symptoms (Mula and Monaco, 2009; Mula *et al.*, 2007).

CASE STUDY

A 37-year-old married female, a housewife with three children, who has been using topiramate 150 mg/day for the last three years due to migraine, presented to our outpatient psychiatric department with complaints of restlessness, irritability and hearing strange voices, which was distressing for the patient. She claimed that the voices resembled the voice of her neighbour, and that they were accusing her of cheating on her husband, saying that she was an immoral person, and commanding her to do things, such as leaving the house. She also complained of insomnia, loss of appetite and trembling, and she said that she could not leave the house. On further questioning, she revealed that six months before she had felt as if her neighbour's husband was spying on her, and that the neighbour's wife became aware of this, and started gossiping about her. Due to all these complaints, the patient failed to complete her daily chores. Her mental status examination revealed signs of irritability, restlessness, and inability to focus attention. She had

numerous auditory hallucinations, e.g. commanding voices or voices talking about her behaviours. Her reality testing was impaired, and she suffered from paranoid delusions and delusions of reference. The patient kept asking for reassurance by saying "There is nothing like that, is there?". She seemed anxious and depressed. She had no insight to her complaints. She also had diminished psychomotor activity. Her psychometric evaluations were as follows: Beck Depression Inventory (BDI) score: 42/63, Beck Anxiety Inventory (BAI) score: 48/63 and Brief Psychiatric Rating Scale (BPRS) score: 48/126.

Topiramate was reduced and discontinued after consultation with a neurologist, and 5 mg of olanzapine bid was prescribed. After two weeks, the patient's anxiety level and the frequency of auditory hallucinations decreased significantly, and she only complained of hearing voices which resembled her father-in-law's. After one month, the patient no longer complained about hearing any voices, and her depressive symptoms decreased as well (BDI score: 17/63, BAI score: 20/63, BPRS score: 8/126).

DISCUSSION

Topiramate is a drug used in epilepsy, migraine prophylaxis, bipolar affective disorder, aggression symptoms observed in borderline personality disorders, post-traumatic stress disorder, eating disorders or weight problems developing secondarily due to the usage of antipsychotics (Alderman *et al.*, 2009; Lieb *et al.*, 2010; Lung *et al.*, 2009; McElroy *et al.*, 2009; Miller and Roache, 2009; Winum *et al.*, 2009). It has been suggested that topiramate may cause psychosis directly or indirectly. In a study conducted by Khan *et al.* (1999), 80 patients were evaluated retrospectively, and it was reported that psychotic symptoms developed about a month after starting topiramate. Five of the patients developed paranoid thoughts, and four patients developed auditory hallucinations. None of these patients had been diagnosed with a psychiatric disorder before.

The mechanism underlying psychotic symptom induction by topiramate is not clear, but a GABAergic hypothesis, involving the inhibition of substantia nigra and overactivity of ascending dopaminergic pathways, has been proposed (Khan *et al.*, 1999). The incidence of topiramate-induced psychosis is reported to be 1.5% (Kanner *et al.*, 2003).

Kober and Gabbard (2005) used topiramate as a regulator of weight loss and mood in an OCD patient and showed that psychotic symptoms developed. Zesiewicz *et al.* (2006) also observed psychotic symptoms after 15 months in two patients with essential tremor who had not received psychiatric treatment before. A patient who used levetiracetam and carbamazepine, and who previously did not have a history of psychosis, developed auditory hallucinations after the addition of 200 mg of topiramate to his treatment (Pasini *et al.*, 2014).

CONCLUSION

Topiramate, which is indicated for the treatment of numerous conditions, is used frequently in psychiatric diseases. In addition to demonstrating positive effects on the outcome of many disorders, it was also observed that the incidence of newly reported psychotic symptoms was 1.5%. It should therefore be used with caution, and patients on topiramate should be closely monitored for psychotic symptoms.

Conflict of interest

The authors do not report any financial or personal links with other persons or organizations, which might affect negatively the content of this publication or claim authorship rights to this publication.

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