



Severe Weight Loss and Emaciation Following Topiramate Administration

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Authors' contributions

This work was carried out in collaboration between all authors. All authors designed the study, wrote the protocol. Author MAH wrote the first draft of the manuscript and managed the literature searches. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Topiramate is an antiepileptic drug, used also for prevention of an episodic migraine. Its effects include sodium-channel-blocking activity, enhancement of cerebral GABA concentrations and antagonism of AMPA/kainate receptors, which leads to a decreased glutamate-mediated excitation. It is documented to possess weight reducing properties. It attenuates appetite through mechanisms that remain to be elucidated. Severe weight loss is not reported in the literature. We investigated one patient with severe weight loss (40.2% loss) resulted in emaciation and found that the implicated drug was topiramate. This notion was confirmed when we discontinued the implicated drug (Topiramate) as the patient regained his weight again to the previously recorded levels. Conclusion: Severe weight loss up to emaciation may occur after topiramate administration,

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Topiramate can be used to counteract the weight gain effect of antipsychotics, long acting topiramate preparation alone or in combination with long acting phentermine can be used to treat morbid obesity.

Keywords: Topiramate; emaciation; weight loss; obesity; epilepsy.

1. INTRODUCTION

Topiramate is an antiepileptic drug, but it has also suggested as a useful agent for preventing episodic migraine and chronic migraine [1-3]. This anticonvulsant has a singular chemical structure and was synthesized during a research project to discover substances analogous to fructose 1,6-diphosphate inhibitors of the gluconeogenic process. Its structural chain resembles a chemical radical in the acetazolamide molecule, which raised the possibility that topiramate possessed anti-epileptic properties [4].

Its effects include sodium-channel-blocking activity, enhancement of cerebral GABA concentrations and antagonism of AMPA/kainate receptors, which leads to a decreased glutamate-mediated excitation [5]. The multiple actions on calcium and sodium voltage channels, and on GABA-A and the kainate/AMPA receptor, also pointed toward its use for migraine prevention [4].

Topiramate is documented to possess weight reducing properties, as well as insulin resistance improving effects [6]. Several studies, including this one, show that topiramate has a strong potential to induce weight loss which is sustained for at least one year.

Topiramate attenuates appetite through mechanisms that remain to be elucidated [7,8]. The combination of phentermine and the antiepileptic topiramate has also been recently approved by the US FDA. The high dose combination of the two medications led to an impressive 7.5–8.7% placebo-adjusted weight loss [7]. Long acting topiramate preparation either alone or in combination with long acting phentermine can be used to treat morbid obesity [9].

The concomitant use of topiramate with antipsychotics in order to prevent weight gain is clinically well known, though not officially sanctioned.

2. CASE REPORT

An informed written consent was obtained from the caregiver for a 24-year old male psychiatric patient to include his medical history, clinical data, and investigations. He is a known case of temporal lobe (TL) epilepsy since adolescence, as indicated by his family, with repeated admissions to our hospital. The presentation of his epileptic seizure is sudden onset aggressiveness, violence toward his father, isolation and visual hallucinations. Interictal EEG was performed and revealed bilateral frontotemporal epileptogenic discharges, Head MRI revealed periventricular white matter foci. Based on these symptoms and investigations the patient was diagnosed as having TL epilepsy, schizophrenia, demyelinating disease. The patient was maintained on the following treatment aripiprazole 15 mg BID, haloperidol 5 mg OD, carbamazepine 200 mg TID, Topiramate 25 mg QID. Observing the patient's weight on admission it was 82 kg surprisingly we found progressive weight loss over 5 months period and his weight dropped to a severe degree (49 kg) about 40.2% loss of his pretreatment weight. The following investigations were done to roll out other causes of emaciation, CBC, ESR, renal function tests, liver function test, thyroid function test, tuberculin test, tumor markers, bone survey, CT chest, CT abdomen, and pelvis, and revealed no abnormalities. When we stopped topiramate, while the other medications were continued, the patient resumed graved appetite and started to gain weight again. His weight reached 57 kg within 1.5 months after discontinuation of Topiramate.

3. DISCUSSION

Severe weight loss following topiramate administration is not reported in the literature following extensive Medline search. In the present case, the patient started to lose weight progressively, inspite of using antipsychotic drugs that proved to result in weight gain. He lost about (40.2%) of his weight. The patient's weight loss was more severe than that reported in meta-analysis study [10] performed on 10 randomized

controlled trials and concluded that topiramate treated group had significant additional weight loss (5.34 kg) compared with placebo-treated group. And also concluded that topiramate treatment increased the chance of clinically significant weight loss (5 and 10%) by more than six fold. Schauer et al. in their study reported 4.7% weight loss in patients receiving topiramate [11]. Tonstad et al. [12] reported significant amounts of weight loss after topiramate intake for 28 weeks as 5.9% in the 96 mg group and 6.5% in the 192 mg group. Another study used high dose combination of antiepileptic topiramate and phentermine (this combination has been recently approved by the US FDA for the treatment of obesity) and concluded that high dose combination of the two medications led to only 7.5–8.7% placebo-adjusted weight loss [7]. Unlike in our case, incoercible topiramate-related vomiting has been reported [13]. In addition, A promising predictor for evaluation weight regain reported by the Verrotti's group and concluded that loss of body weight is a reversible effect after TPM discontinuation and that homeostatic model assessment of insulin resistance HOMA-IR is the only predictive factor of weight regain [14]. This will open the door for new researches to predict patients who may lose and regain weight after topiramate intake and discontinuation.

4. CONCLUSION

Severe weight loss up to emaciation may occur after prolonged topiramate administration.

Topiramate can be used to counteract the weight gain effect of antipsychotic drugs.

CONSENT

An informed written consent was obtained from the caregiver to use anonymously the patient's data, clinical examination, investigations and treatment.

ETHICAL APPROVAL

This study was approved by the local ethical committee in the hospital.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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