Can topiramate reduce nightmares in posttraumatic stress disorder?

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Re-experiencing a previous life-threatening stress through nightmares or recurrent memories is a hallmark of posttraumatic stress disorder (PTSD). In the United States, the lifetime risk of PTSD is 10.1% and the 12-month prevalence is 3.7%.1 The selective serotonin reuptake inhibitors (SSRIs) sertraline and paroxetine are FDA-approved for treating PTSD; clinicians commonly use any SSRI for this disorder. Although SSRIs can alleviate many PTSD symptoms, at times patients experience only a partial response, which necessitates other interventions.

**Rationale for using topiramate**

The anticonvulsant topiramate blocks voltage-sensitive sodium channels, augments γ-aminobutyric acid type A, antagonizes the glutamate receptor, and inhibits carbonic anhydrase. Researchers have hypothesized that limbic nuclei become sensitized and “kindled” after exposure to a traumatic event. Anticonvulsants such as topiramate may help mitigate stress-activated kindling in PTSD.2,3

**What does the evidence say?**

Although less compelling than double-blind, placebo-controlled trials, small open-label studies and some case reports indicate a potential role for topiramate in PTSD for specific populations.4,5 In an 8-week open-label study, Alderman et al4 found adjunctive topiramate led to a statistically significant reduction in Clinician-Administered PTSD Scale (CAPS) scores and nightmares in 43 male veterans with combat-related PTSD. There was a nonsignificant decrease in high-risk alcohol use.

In a 2002 retrospective case series, Berlant et al7 found topiramate as monotherapy or adjunctive therapy reduced nightmares in 35 patients with chronic, non-combat PTSD. Nightmares decreased in 79% of patients and flashbacks decreased in 86%, with symptom improvement in a median of 4 days. Limitations of this study included lack of placebo control, a low number of participants, and a high dropout rate (9/35).

Two years later, Berlant8 used the PTSD Checklist-Civilian version (PCL-C) to assess response to topiramate in an open-label study of 33 patients with chronic, non-hallucinatory PTSD. Twenty-eight patients used topiramate as add-on therapy. PCL-C scores decreased by ≥30% in 77% of patients in 4 weeks, with a median dose of 50 mg/d and a median response time of 9 days.

In a double-blind, placebo-controlled trial, Tucker et al9 assessed 38 civilian patients who took topiramate monotherapy for PTSD. Using the CAPS, researchers concluded that topiramate reduced re-experiencing symptoms, but the effect was not statistically significant.9

Lindley et al10 conducted a randomized, double-blind, placebo-controlled trial to study the effect of add-on topiramate in 40 patients with chronic, combat-related PTSD. Because many patients in this study had a history of depression and substance use disorders, topiramate was added to antidepressants; no anticonvulsants, antipsychotics, or benzodiazepines were used. Similar to previous studies, researchers found no statistically significant effect on PTSD symptom severity or global symptom improvement. However, the small number of participants and a high dropout rate limited this study.10

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In a 12-week, double-blind, placebo-controlled study of 35 men and women age 18 to 62 with PTSD, Yeh et al found that topiramate (mean dose: 102.94 mg/d) lead to a statistically significant overall CAPS score reduction, with significant improvements in re-experiencing symptoms, such as nightmares.

Our opinion

FDA-approved treatments such as SSRIs should be the first pharmacologic intervention for PTSD. If a patient’s response is partial or inadequate, consider additional treatment options. For patients with persistent re-experiencing symptoms, evidence and experience with prazosin and trazodone are more robust than that for topiramate.12

Using topiramate to reduce re-experiencing symptoms such as nightmares in PTSD is not supported by statistically significant evidence from double-blind, placebo-controlled trials. However, numerous open-label studies and case reports suggest that there may be a role for topiramate in PTSD patients who do not respond to other treatments. Data indicate that topiramate may be helpful for PTSD patients who have high-risk alcohol use or migraine headaches.13

Because some patients who take topiramate lose weight, the medication may be useful for PTSD patients who are overweight.13

References


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