Think beyond prazosin when treating nightmares in PTSD

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Nightmares are a common feature of posttraumatic stress disorder (PTSD) that could lead to fatigue, impaired concentration, and poor work performance. The α-1 antagonist prazosin decreases noradrenergic hyperactivity and reduces nightmares; however, it can cause adverse effects, be contraindicated, or provide no benefit to some patients. Consider these alternative medications to reduce nightmares in PTSD.

Alpha-2 agonists

Clonidine and guanfacine are α-2 agonists, used to treat attention-deficit/hyperactivity disorder and high blood pressure, that decrease noradrenergic activity, and either medication might be preferable to prazosin because they are more likely to cause sedation. A review and a case series showed that many patients—some with comorbid traumatic brain injury—reported fewer nightmares after taking 0.2 to 0.6 mg of clonidine.[1,2] Guanfacine might be more beneficial because it has a longer half-life; 2 mg of guanfacine eliminated nightmares in 1 patient.[3] However, in a double-blind placebo-controlled study and an extension study, guanfacine did not reduce nightmares or other PTSD symptoms.[4,5]

Initiate 0.1 mg of clonidine at bedtime, and titrate to efficacy or to 0.6 mg. Similarly, initiate guanfacine at 1 mg, and titrate to efficacy or to 4 mg. Monitor for hypotension, excess sedation, dry mouth, and rebound hypertension.

Cyproheptadine

Used to treat serotonin syndrome, cyproheptadine's antagonism of serotonin 2A receptors has varying efficacy for reducing nightmares. Some patients have reported a decrease in nightmares at dosages ranging from 4 to 24 mg.[1,6] Other studies found no reduction in nightmares or diminished quality of sleep.[1,7]

Initiate cyproheptadine at 4 mg/d, titrate every 2 or 3 days, and monitor for sedation, confusion, or reduced efficacy of concurrent serotonergic medications. Cyproheptadine might be preferable for its sedating effect and potential to reduce sexual adverse effects from serotonergic medications.

Topiramate

Topiramate is approved for treatment of epilepsy and migraine headache. At 75 to 100 mg/d in a clinical trial, topiramate partially or completely suppressed nightmares.[8] Start with 25 mg/d, titrate to efficacy, and monitor for anorexia, paresthesias, and cognitive impairment. Topiramate might be better than prazosin for patients without renal impairment who want sedation, weight loss, or reduced irritability.

Gabapentin

Gabapentin is approved to treat seizures and postherpetic neuralgia and also is used to treat neuropathic pain. When 300 to 3,600 mg/d (mean dosage, 1,300 mg/d) of gabapentin was added to medication regimens, most patients reported decreased frequency or intensity of nightmares.[9] Monitor patients for sedation, dizziness, mood changes, and weight gain. Gabapentin might be an option for patients without renal impairment who have comorbid pain, insomnia, or anxiety.

Are these reasonable alternatives?

Despite small sample sizes in published studies and few randomized trials, clonidine, guanfacine, cyproheptadine, topiramate, and gabapentin are reasonable alternatives to prazosin for reducing nightmares in patients with PTSD.

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Consider gabapentin for patients without renal impairment who have comorbid pain, insomnia, or anxiety