

Terazosin for the Treatment of Trauma-Related Nightmares: A Report of 4 Cases

Anjali Nirmalani-Gandhy, MD, Deborah Sanchez, MD, MPH, and Glenn Catalano, MD

Abstract: The selective α_1 -adrenergic antagonist prazosin has been shown in multiple studies to be effective in targeting trauma-related nightmares in posttraumatic stress disorder. There are limited data regarding the effectiveness of another selective α_1 -adrenergic antagonist terazosin for the treatment of trauma-related nightmares. We present 4 cases in which terazosin was effectively used to treat nightmares as a second-line agent after prazosin failure. Further studies are needed to validate terazosin as an alternative to prazosin for the treatment of posttraumatic stress disorder-related nightmares.

Key Words: terazosin, nightmares, posttraumatic stress disorder

(*Clin Neuropharm* 2015;38: 00–00)

Prazosin and terazosin are selective α_1 -adrenergic antagonists that are traditionally used to treat hypertension and benign prostatic hypertrophy.^{1,2} Although not Food and Drug Administration–approved for this use, the efficacy of centrally active prazosin to target trauma-related nightmares in posttraumatic stress disorder (PTSD) is well documented.^{3–5} The neurobiological rationale for exploring α_1 -adrenergic antagonist therapy includes the distribution of α_1 -receptors in the hippocampus and amygdala, and the involvement of α_1 -adrenergic receptors in the modulation of sleep and startle.^{6–8} The hyperresponsiveness in PTSD suggests that blocking central nervous system postsynaptic adrenergic receptors could be an effective treatment.^{9,10} Although there have been many studies on the use of prazosin for trauma-related nightmares, there are limited data on terazosin use.^{11,12} We present 4 cases in which terazosin was effectively used as a second-line treatment after prazosin failure.

CASE REPORTS

Case 1

The patient was a 47-year-old white male combat veteran with PTSD who presented in 2008, while still on active duty, with symptoms of nightmares, insomnia, avoidance, hypervigilance, depressed mood, and irritability. Two years prior, he had experienced loss of consciousness, concussion, and cervical spine injury secondary to an improvised explosive device explosion. He was initially treated with zolpidem 10 mg every night at bedtime. Two years later, citalopram 40 mg daily and trazodone 50 mg every night at bedtime were tried but were discontinued because of lack of efficacy and adverse effects. At the time of the patient's first visit, he was being treated with zolpidem 10 mg as well as his baseline medications of rosuvastatin 10 mg daily, aspirin 81 mg daily, fish oil 1 mg twice daily, hydrochlorothiazide

(HCTZ)/lisinopril 12.5 mg/10 mg daily, and omeprazole 20 mg daily. He was started on prazosin 1 mg nightly, which was able to be titrated up to 4 mg nightly as tolerated. The patient stopped at 2 mg because of some dizziness when he took it in the evening. At the next visit, prazosin 1 mg in the morning was added to the 2 mg evening dose. Sertraline 50 mg daily was also initiated. He was not able to tolerate the additional prazosin in the morning but did find some benefit to the prazosin 2 mg nightly, in that he was able to sleep an additional hour at night (4 hours rather than 3). He was still having nightmares most nights. The patient discontinued taking sertraline because he felt that it increased his irritability. He was started on venlafaxine immediate release, which was titrated up to 150 mg twice daily, and buspirone 5 mg three times a day as needed, which did help reduce his irritability and anxiety. Over the next few months, zolpidem 10 mg every night at bedtime was changed to eszopiclone 3 mg every night at bedtime, which was not effective in increasing the amount of sleep or reducing nightmares. Two months later, while still on eszopiclone, venlafaxine, and buspirone, the prazosin was discontinued because of reported increase in nightmares. Terazosin 2 mg was initiated in its place and titrated up to 4 mg nightly. He came back 4 months later reporting that his nightmares were now “dull” and no longer as distressing when he woke up. He was still having nightmares most nights and still only getting 3 to 4 hours of sleep at night. We changed his eszopiclone to zolpidem sustained action 12.5 mg every night at bedtime, which seemed to help with the quality of his sleep although he was still getting only 4 hours. Over the next several months, terazosin was titrated to 2 mg every morning and 10 mg nightly, which reduced his nightmare frequency to 2 times a week from daily. The patient reported that the addition of the 2 mg in the morning helped him feel “calmer.” The patient denied any adverse effects such as dizziness with the terazosin, and after 2 years of working on symptom reduction with medication, he was able to start a modified prolonged exposure program to address his core PTSD symptoms.

Case 2

The patient was a 67-year-old white male combat veteran with PTSD who presented in 2010 with symptoms of nightmares and decreased quantity of sleep. He was taking HCTZ/lisinopril 25 mg/20 mg daily as his only baseline medication, with occasional low blood pressure readings on this dose. In coordination with his primary care provider, the HCTZ/lisinopril dose was reduced to 12.5 mg/10 mg daily, and he was started on prazosin 1 mg nightly, which helped reduce the frequency of nightmares from nightly to 2 times a week. When the prazosin dose was increased to 2 mg to further reduce nightmares, the patient was unable to tolerate the dose due to several low blood pressure readings and dizziness. His primary care provider changed his blood pressure medication from the combination HCTZ/lisinopril to just HCTZ 25 mg daily; this allowed the patient to tolerate prazosin 2 mg nightly, which worked well for his nightmares. He denied having nightmares with this dose and was able to sleep 7 hours per night. Citalopram 20 mg daily was added to his medication

James A. Haley Veterans' Hospital, Tampa, FL.

Address correspondence and reprint requests to Anjali Nirmalani-Gandhy, MD, James A. Haley Veterans' Hospital, 13000 Bruce B. Downs Blvd, 116-A, Tampa, FL 33612; E-mail: Anjali.Nirmalani-Gandhy@va.gov

Conflicts of Interest and Source of Funding: The authors have no conflicts of interest to declare.

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DOI: 10.1097/WNF.0000000000000077

regimen once he was stable on the prazosin, which was helpful for his mood and irritability. About a year later, his primary care put him back on HCTZ/lisinopril 12.5 mg/10 mg daily because of poorly controlled blood pressure on HCTZ 25 mg alone. The patient reported dizziness with taking the prazosin soon after this and stopped the prazosin, which resulted in a resolution of the dizziness. Over the next several months, the patient reported increasing frequency of nightmares and depressed mood. His citalopram was increased to 30 mg and moved to nightly, which did help with sleep but not with his mood or nightmares. The patient refused further titration of citalopram because of concerns about cardiac conduction problems. Citalopram was tapered off, and sertraline was initiated and titrated up to 100 mg daily without complaints. He continued to report nightmares nightly and was started on terazosin 2 mg nightly. The patient reported good effects with the terazosin 2 mg having only “rare nightmares,” of which he does not remember the content. He was now able to sleep 9 hours per night. He has been on the same 2 mg dose of terazosin for 2 years with stability of effect. The patient reported some dizziness with the terazosin but denies any significant hypotensive episodes similar to what was occurring when he was taking prazosin.

Case 3

The patient was a 49-year-old Asian female combat veteran who presented to our clinic for treatment of PTSD. Her symptoms included depressed mood, difficulty initiating sleep due to apprehension and fears that the home was not safe, and nightmares associated with autonomic arousal and fear, with the inability to return to sleep due to anxiety. The patient also reported that she began to drink nightly to facilitate sleep while deployed. The patient reported a past history of 4 suicide attempts; the most recent attempt was 4 months before her initial evaluation with us. Before presenting to our clinic, she had tried bupropion sustained release 150 mg twice daily for 1 month, which was discontinued because of worsening depression, and trazodone 50 mg nightly for a few days, which caused a rash. At presentation, she had stopped drinking for 3 weeks and recently started 60 mg of citalopram daily and hydroxyzine 50 mg nightly, which were effective for her mood and anxiety but not for her difficulty with sleep initiation or nightmares. Prazosin 1 mg nightly was started and titrated up to 1 mg twice daily with good effect for nightmares but not for prolonged sleep latency. The patient was lost to follow-up for about 10 months, during which time she ran out of medication and began to drink alcohol nightly again to sleep. Citalopram was restarted and titrated up to 40 mg daily, and prazosin was started at 1 mg twice daily. The patient did not want to continue hydroxyzine; therefore, trazodone was retried at 25 mg nightly. On return visit, she reported improved sleep but she was having nightmares every night. She was able to reduce her alcohol use to 2 or 3 drinks on the weekend only. She continued to report significant anxiety. An increase in prazosin to 2 mg twice daily was tried and was effective for nightmares, but the patient reported some “cloudiness” during the day. Eventually, the patient could not tolerate this adverse effect, noting she “felt sick all the time” and discontinued the prazosin. The patient returned for follow-up 6 months later reporting the nightmares had returned with increased intensity and frequency. With the increase in symptoms, the patient started to drink alcohol nightly. Terazosin 2 mg nightly was initiated at this visit. At the subsequent visit, the patient reported that her nightmares had resolved completely. She was, however, still drinking up to 5 drinks a night. We started naltrexone 50 mg to help with the alcohol cravings. The patient reported good response to naltrexone with being able to cut back on drinking to 2 or 3 a week, if she drank at all. Nightmares,

sleep, and anxiety continued to be well controlled on terazosin, citalopram, and trazodone.

Case 4

The patient was a 49-year-old biracial (African American and white) combat veteran with PTSD who had been treated with therapy and sertraline 200 mg daily and lorazepam 0.5 mg three times a day as needed with less than optimal effects. At initial evaluation, he reported good control of irritability with initiation of sertraline; however, he continued to struggle with nightmares most nights, poor sleep, and avoidance of crowds and interacting with others. He was started on prazosin 1 mg twice daily for hyperarousal and nightmares, and the lorazepam was discontinued. At follow-up, he reported an improvement in nightmares, but the hyperarousal symptoms in the evening were still excessive. Prazosin was increased to 1 mg every morning and 2 mg nightly. At next visit, he reported modest improvement in nightmares and hyperarousal, but irritability was becoming more of an issue. Therefore, sertraline was increased to 250 mg every morning. At follow-up, he reported good response to the increase in sertraline but nightmares continued to occur twice a week with high intensity and motoric activity (described as swinging and punching in his sleep). Prazosin was further increased to 1 mg every morning and 4 mg nightly to address this. He was not able to tolerate 4 mg of prazosin in the evening because of orthostatic hypotension, so he adjusted his prazosin to 1 mg in the morning, 2 mg at noon, and 2 mg in the evening, which was more tolerable. The patient was compliant with this regimen but continued to note difficulty with sleep. Zolpidem 10 mg every night at bedtime was added, which was effective in increasing the quantity of sleep to 6 hours a night. Two months later, the patient returned for follow-up, reporting daytime drowsiness associated with regular zolpidem use and dizziness associated with daytime dosing of prazosin. He reported an increase in nightmares as well. The decision was made to cross taper the patient off of prazosin and on to terazosin. Terazosin was initiated at 2 mg every night at bedtime. He noted good tolerability with reduction in nightmares. He continued on this regimen of sertraline 250 mg, terazosin 2 mg, and zolpidem 10 mg for the next year. After about 1 year, buspirone 5 mg three times a day was added to address generalized anxiety during the day, with good effect. About 16 months later, he reported an increase in nightmares, including an increase in motoric activity, despite compliance with medication. His terazosin dose was initially increased to 4 mg every night at bedtime, with minimal improvement in symptoms. His dose was then increased to 6 mg every night at bedtime, which was both well tolerated and effective. The patient reported that the nightmares were reduced from nightly to once a week, which was tolerable.

DISCUSSION

To our knowledge, there is currently only 1 case report and 1 poster presentation in the literature regarding the use of terazosin for PTSD-related nightmares.^{11,12} The poster presentation described an open-label trial of terazosin for PTSD. Patients were treated with terazosin at doses between 3 and 7 mg daily and were noted to have reduced Clinician-Administered PTSD Scale scores and fewer distressing dreams. The case report described a 27-year-old woman whose PTSD-related sleep disturbances improved with terazosin 2 mg daily.

Although both prazosin and terazosin are α_1 -adrenergic antagonists, there are differences between them. Prazosin is a highly lipophilic α_1 -receptor antagonist; as such, it enters the

brain more easily from the blood and is centrally active.^{13,14} Prazosin is well absorbed but undergoes substantial first-pass metabolism. It has a short half-life of 2 to 3 hours and reaches peak plasma concentrations within 1 to 2 hours. Terazosin is longer acting, with a half-life of approximately 12 hours; it reaches peak plasma concentrations in 1 hour. It undergoes little first-pass metabolism; almost all the circulating dose is in the parent form of the drug.¹⁵ The adverse effect profiles of prazosin and terazosin are similar; adverse effects tend to be infrequent and mild, and can include dizziness, palpitations, headache, and fatigue.¹⁶ In the cases we presented, prazosin was initially effective in targeting sleep-related symptoms of PTSD, yet ultimately it was discontinued because of tolerability issues. In these patients, terazosin was initiated as a second-line treatment, and a temporal relationship was noted with respect to positive therapeutic response to terazosin.

This case series suggests that terazosin may be a useful therapeutic option to target trauma-related nightmares in individuals who do not tolerate prazosin because of adverse effects. The limited data currently available in the literature suggest that there may be a role for terazosin in the treatment of PTSD-related sleep disturbance; however, there are currently no placebo-controlled, double-blind studies or long-term studies to assess its efficacy and tolerability for this use. More studies would help determine if terazosin is a viable alternative to prazosin for the treatment of PTSD-related nightmares.

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