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Prazosin dosed 3 times a day to treat flashbacks related to PTSD: A case report

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Abstract

Prazosin is an alpha-1 adrenergic receptor antagonist widely known by mental health providers for its off-label use for nightmares in patients with PTSD. Prazosin is lipophilic and crosses the blood-brain barrier to antagonize alpha-1 receptors in the central nervous system, potentially reducing autonomic arousal caused by PTSD. There have been numerous case reports describing the reduction of nightmares and daytime flashbacks due to PTSD with prazosin dosed at night and during the day, respectively. This case report illustrates the resolution of flashbacks related to chronic PTSD with prazosin dosed 3 times a day. As the half-life of prazosin is only 2 to 3 hours, even a twice daily dosing regimen may lead to breakthrough symptoms between doses. This case proposes a unique dosing strategy for prazosin and need for further research utilizing multiple daily doses of prazosin in the treatment of PTSD.

Keywords: posttraumatic stress disorder, PTSD, nightmares, trauma, flashbacks, hypervigilance, psychiatry, prazosin

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Background

PTSD is a psychiatric disorder with several characteristic symptoms including flashbacks, nightmares, avoidance, and hypervigilance due to trauma(s).[1] A common off-label treatment for PTSD is prazosin, a competitive alpha-1 adrenergic antagonist approved by the US FDA for management of hypertension. It is proposed that prazosin reduces nightmares related to PTSD by inhibiting adrenergic stimulation and hyperarousal in the central nervous system. Because of prazosin's half-life of 2 to 3 hours, it is generally dosed 2 to 3 times per day when treating hypertension but is usually dosed once a day at bedtime to treat nightmares related to PTSD.[2] Although the duration of action for prazosin is 10 to 24 hours, the peak effect is only 2 to 4 hours, leading to the need for multiple daily doses to achieve maximum benefit.[3] A potential serious adverse effect of prazosin is *first-dose hypotension* which has been minimized in PTSD clinical trials by using a small starting dose of 1 mg and slow titration of 1 mg every few days on average.[4]

Randomized controlled trials of prazosin to treat PTSD have had inconsistent results. A 2013 trial[5] of prazosin for active-duty soldiers with PTSD showed reduction in nightmares and hyperarousal symptoms as well as improvement in sleep quality and global function. However, another similar trial[6] in 2018 using prazosin

TABLE: Patient's medication list upon intake to the psychiatry clinic

Medication	Dosage Regimen	Indication
Fluoxetine 10 mg	3 capsules PO daily with breakfast	PTSD
Albuterol-ipratropium 2.5 mg-0.5 mg/3 mL solution	3 mL by nebulizer QID	Asthma
Roflumilast 500 mcg	1 tablet PO daily	Asthma
Ciprofloxacin-hydrocortisone otic 0.2%/1% suspension	3 drops in left ear BID for 7 days	Ear infection
Omeprazole 40 mg delayed release	1 capsule PO daily	GERD

BID = twice daily; GERD = gastroesophageal reflux disease; PO = by mouth; QID = 4 times a day.

for veterans with chronic PTSD and frequent nightmares showed no reduction in nightmares or improvement in sleep quality. In addition to veteran studies, a placebo-controlled study[7] showed that prazosin reduces nightmares in civilians with PTSD associated with traumas such as childhood sexual and physical abuse. While there have been 6 placebo-controlled clinical trials showing prazosin can reduce PTSD-related nightmares, only 1 trial had a twice daily dosing regimen.[5] To our knowledge, no studies have evaluated dosing prazosin 3 times a day to target daytime PTSD symptoms in individuals with predominant flashbacks. This case report examines a patient with PTSD experiencing severe and distressing flashbacks that is successfully treated with prazosin dosed 3 times a day.

Case Report

A 59-year-old White female with a past psychiatric history of PTSD, bipolar II disorder, and alcohol use disorder (in sustained remission) presented for intake to our psychiatric outpatient clinic via telemedicine with the chief complaint of worsening anxiety for the past 3 months. Her past psychiatric medication history included bupropion, quetiapine, sertraline, diazepam, and alprazolam. She reported taking these medications over the past 30 years but could not recall dose, frequency, or duration of these trials, and no prior records were available. She did note that these medications were not very helpful for her PTSD symptoms in the past. On intake, current medications included fluoxetine 30 mg daily with breakfast as off-label monotherapy for PTSD, which had been prescribed by her primary care provider for the past 5 years. Past medical history included asthma, gastroesophageal reflux disease, and a recent ear infection that was being treated; all treatments for these indications are listed in the Table.

On intake, the patient was calm and cooperative with linear thought process, normal rate of speech, and labile affect. She reported vivid flashbacks of prior sexual, physical, and emotional abuse, and requested help coping with them. She had just started trauma-focused therapy 1 month prior because of difficulty coping with her PTSD symptoms but was having difficulty talking about her trauma because of triggering of flashbacks. The patient reported depressed mood, anxiety, anger, generalized fear and isolation, hearing a voice in her head at times "saying good things," and she was spontaneously laughing, crying, and cursing. She denied suicidal ideation, homicidal ideation, nightmares, or visual hallucinations. She also reported only getting 2 hours of sleep at night but was afraid to sleep more, despite always feeling exhausted, because of feeling vulnerable. She reported periods of high energy in the distant past where she would clean her house often and have fast speech. She denied a history of psychiatric hospitalization or suicide attempts. Although the patient had a labile mood and history of bipolar II disorder, she did not meet *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5) criteria for a hypomanic episode as there were no signs of grandiosity, decreased need for sleep, pressured speech, flight of ideas, distractibility, increased goal-directed activity, or involvement in activities with potentially painful consequences. However, she did meet DSM-5 criteria for PTSD, and the psychiatrist prescribed her prazosin 1 mg in the morning for flashbacks since she denied nightmares. Her blood pressure and heart rate 2 weeks prior to the intake were recorded as 130/80 mm Hg and 74 beats/min, respectively, and she was counseled about the risk of first-dose hypotension. Fluoxetine 30 mg daily was continued with no changes.

Two months later at follow-up, the patient reported that her morning flashbacks had completely resolved within a few days after starting prazosin 1 mg daily at 8:00 AM, but she was still having flashbacks in the afternoon and evening. She also reported hearing voices in her head at night that were "trauma-related" and was still only sleeping 2 hours per night. She denied any adverse effects from the medication. The psychiatrist increased her prazosin dose to 1 mg 3 times a day (8:00 AM, 1:00 PM, and 5:00 PM) and continued fluoxetine 30 mg daily.

One month later, the patient returned to the clinic reporting she was no longer hearing voices or having flashbacks. She also no longer felt vulnerable at night and was now sleeping 8 hours per night consistently. She reported having more energy but denied excessive energy, euphoria, or rapid speech. Trauma therapy was progressing well as she no longer had reexperiencing symptoms when talking about her trauma. The lowest blood pressure recorded by the patient's primary care physician was 102/58 mm Hg 5 days after increasing prazosin to 3 times daily, but she denied any

physical symptoms. Her blood pressure and heart rate were recorded as 120/80 mm Hg and 78 beats/min, respectively, the week prior to this follow-up. No changes were made to the patient's medication regimen of prazosin 1 mg 3 times a day and fluoxetine 30 mg daily.

Nine months after starting prazosin dosed 3 times a day, the patient denied feeling depressed or anxious, having flashbacks, hearing voices, difficulty sleeping, or medication side effects. She saw her therapist regularly and was able to work through her traumatic experiences without flashbacks. She requested to continue prazosin 1 mg 3 times a day as she did not want to risk her symptoms returning. There were no self-rated or standardized clinical scales used, but rather subjective reports by the patient over this period of 9 months.

Discussion

According to the US Department of Veteran Affairs,[8] first-line medications for PTSD are the SSRIs sertraline, fluoxetine, and paroxetine, and the SNRI venlafaxine. Although only paroxetine and sertraline are FDA-approved for PTSD, fluoxetine is often prescribed as off-label monotherapy as it has been shown to reduce PTSD symptoms.[8,9] In this report, the patient was prescribed fluoxetine 30 mg daily for PTSD for 5 years and began to have worsening of PTSD symptoms over 3 months. Although the fluoxetine dose could have been increased on intake, SSRIs can take 4 to 6 weeks for initial response and up to 6 to 9 months to see full benefit when treating PTSD.[10] Thus, the psychiatrist chose to initiate a morning dose of prazosin to address the patient's flashbacks.

We propose the resolution of flashbacks allowed the patient in this case to gain full benefit of trauma-based therapy. In a placebo-controlled study of civilians with PTSD, daytime pretreatment with prazosin reduced psychological distress to trauma cues.[11] This gives evidence that daytime dosing of prazosin could reduce psychological distress that can arise in trauma-based therapy. The patient started trauma-based therapy 1 month prior to starting prazosin, which also likely contributed to the improvement of PTSD symptoms. However, she was not able to participate fully in therapy until her flashbacks resolved with multiple daily doses of prazosin. There was likely an overall synergistic effect between prazosin and trauma-based therapy in this situation.

The patient in this case report only needed 3 mg/d divided in 3 doses for resolution of flashbacks. Although the average beneficial dose of prazosin in clinical trials with veteran populations are more than 10 mg at night, in a civilian study the average daily dose of prazosin at bedtime to reduce nightmares was 3.1 mg ± 1.2 mg.[5,6,7] The patient's flashbacks were reduced with prazosin 1 mg in the morning; however, she felt the effects were wearing off in the afternoon. As the peak effect of prazosin is at 2 to 4 hours, it would stand to reason that it would need to be dosed multiple times a day to be fully effective.

Conclusion

In this case report, the patient's PTSD symptoms were significantly improved with prazosin dosed multiple times a day and with no adverse effects. In addition, the patient had an improved experience in trauma-based therapy because of no longer having flashbacks when talking about her trauma. This case shows that although classically dosed at bedtime to treat nightmares, prazosin was used in multiple daily doses to successfully treat flashbacks. More clinical trials of prazosin dosed multiple times a day are needed to validate this dosing strategy.

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