May 2nd, 12:00 AM

Doxazosin Immediate Release as Alternative Treatment for Nightmares in Post-Traumatic Stress Disorder: A Case Report

Danyaal Khan
Rowan University

Christie Richardson
Rowan University

Martin Forsberg
Rowan University

Doxazosin Immediate Release as Alternative Treatment for Nightmares in Post-Traumatic Stress Disorder: A Case Report

ROWAN-VIRTUA School of Osteopathic Medicine

Danyaal Khan BS, Christie Richardson DO, MS, Martin Forsberg MD

Department of Psychiatry

Introduction

PTSD

Post-traumatic stress disorder (PTSD) is a mental health disorder which is characterized by exposure to a traumatic event with subsequent avoidance, autonomic symptoms, intrusion symptoms (nightmares, flashbacks, etc.), and alterations in mood, cognition, arousal, and reactivity for at least one month (1). PTSD may result after experiencing a life-threatening or horror-inducing event such as exposure to war, combat, sexual violence, etc, and is a fairly common diagnosis worldwide. The National Comorbidity Survey in 1995 studied a sample of 5,877 individuals aged 15 to 54 years in the United States and found an overall lifetime PTSD prevalence rate of 7.8% with rates for women at 10.4% and men at 5.0% (2). First-line treatments for PTSD involve psychological therapy and pharmacological interventions, which are commonly used in conjunction. Therapies include cognitive processing therapy, exposure therapy, trauma-focused therapy, psychodynamic therapies, cognitive behavioral therapy and family therapy. (3) First-line pharmacological interventions mainly include selective-serotonin reuptake inhibitors (SSRI's) such as fluoxetine, paroxetine, and sertraline, and serotonin-norepinephrine reuptake inhibitors (SNRI's) such as venlafaxine. Sertraline and paroxetine are the only medications approved by the US Food and Drug Administration (FDA) for the management of PTSD (6).

Prazosin and Doxazosin

Prazosin, an alpha-1 adrenergic antagonist, which is FDA approved for hypertension and benign prostatic hypertrophy, has historically been used off-label in PTSD for treatment of nightmares, hyperarousal and autonomic symptoms (4). Recently, there have been case reports and studies using doxazosin XL (extended release), another alpha-1 adrenergic antagonist, in the treatment of PTSD. Doxazosin IR (immediate release) has been of interest to us due to its longer half-life of 15-19 hours compared to prazosin's half-life of 3 hours and its lower available starting dose (1 mg vs. 4 mg) (7).

Purpose

In this case report, we present a patient diagnosed with PTSD who was initially treated with prazosin with reduction in trauma-related nightmares. In this report, doxazosin IR was prescribed in place of prazosin and had just as much benefit. We suggest that doxazosin IR has a long enough half-life to be dosed once a day to treat both daytime and nighttime symptoms of PTSD, which has not been documented in the literature that we know of. Using this formulation may be especially useful for patients who cannot tolerate the higher dosage that the XL formulation has available.

Case Report

A 72-year-old male with a past psychiatric history of PTSD, obsessive compulsive disorder, and schizoaffective disorder, bipolar type, presented to our outpatient clinic with flashbacks, hypervigilance, nightmares and insomnia. He had a history of abuse which manifested into persecutory and intrusive nightmares that greatly affected psychosocial functioning. At the time he was prescribed sertraline 200 mg daily, valproic acid 100 mg twice daily, aripiprazole 10 mg daily and clonazepam 1 mg three times a day. He was also concurrently being treated with cognitive behavioral therapy. We started prazosin which was eventually titrated to 2 mg three times a day, which led to, in the patient's words, "90% less nightmares."

Case Report Cont.

Four years after beneficial treatment with prazosin, the patient experienced psychiatric decompensation after aripiprazole was reduced, and while hospitalized, prazosin was discontinued due to concern for polypharmacy. Once discharged from the hospital, we restarted a lower prazosin dose of 1 mg twice daily to prevent recurrence of PTSD symptoms, but eventually switched to doxazosin IR eight months later due to an increase in PTSD symptoms. Our reasoning for this was the opportunity to dose doxazosin daily rather than dose prazosin multiple times a day. Other medications on doxazosin initiation included sertraline 250 mg daily, tamsulosin 0.4 daily, melatonin 5 mg nightly, quetiapine 50 mg daily, afternoon, and 100 mg nightly, and aripiprazole 10 mg daily. Two months later, the patient described reduction in nightmares, no flashbacks, improved sleep, and denied dizziness. Doxazosin IR was titrated to 4 mg nightly, and after more than two years, the patient continued to report remission of nightmares.

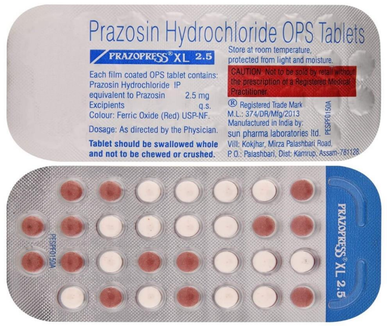
Figures/Tables

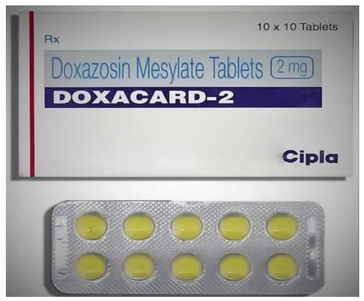
Table 1: Treatment of prazosin versus doxazosin IR

Final dose of prazosin	Reported reason for prazosin discontinuation	Final dose of doxazosin IR
2 mg TID	To reduce polypharmacy	4 mg HS

HS: nightly; TID: three times a day

Table 2: Prazosin vs Doxazosin IR





Prazosin	Doxazosin
• Half life is 2-3 hours • Duration of action of 6-10 hours • Can require multiple daily dosing • Common side effects are drowsiness, palpitations, and nausea	• IR and XL formulation half-lives are 22 hours • Duration of action over 24 hours • Can be dosed once daily • Common side effects are dizziness, headache, and edema

Discussion

Doxazosin is an alpha-1 adrenergic antagonist that is FDA approved to treat hypertension and benign prostatic hyperplasia (12). It is theorized that alpha-1 adrenergic antagonists reduce the burden of stress effects on the hypothalamic-pituitary-adrenal axis and norepinephrine surge during stressful events, which may reduce arousal symptoms in PTSD. Due to doxazosin being in the same class as prazosin, which has had off-label success in treating trauma-related nightmares, there is much interest in its efficacy given its longer half-life. Doxazosin differs from prazosin in that it has a smaller side effect profile and a longer half life of 22 hours versus 2-3 hours for prazosin (13). Doxazosin has a better absorption profile which reduces risk for the adverse effect of hypotension (15).

In our case report, the patient was initially treated with prazosin with remission of PTSD-related nightmares, but the medication was discontinued due to concern for polypharmacy. Doxazosin IR was initiated in this patient due increase of PTSD nightmares symptoms, which was successful in place of prazosin without adverse effects. This patient had benefit with 3:2 of prazosin to doxazosin dose.

This case report serves to provide important insight into the possible use of doxazosin IR as a treatment in trauma-related nightmares. Although not specifically analyzed in this case report, we theorize that doxazosin's longer half-life compared to prazosin can reduce trauma-related daytime arousal symptoms with once daily dosing. Further studies and research on doxazosin IR use to treat trauma-related symptoms is recommended.

Conclusion

We present this case to suggest for doxazosin IR to be utilized for PTSD arousal symptoms, specifically nightmares, given its convenient once daily dosing in comparison to prazosin.

References

1. Compean, E., & Hamner, M. (2019). Posttraumatic stress disorder with secondary psychotic features (PTSD-SP): Diagnostic and treatment challenges. *Progress in neuro-psychopharmacology & biological psychiatry*, *88*, 265–275. https://doi.org/10.1016/j.pnpbp.2018.08.001
2. Keane, T. M., Marshall, A. D., & Taft, C. T. (2006). Posttraumatic stress disorder: etiology, epidemiology, and treatment outcome. *Annual review of clinical psychology*, *2*, 161–197. https://doi.org/10.1146/annurev.clinpsy.2.022305.095305
3. Friedman M. J. (1996). PTSD diagnosis and treatment for mental health clinicians. *Community mental health journal*, *32*(2), 173–193. https://doi.org/10.1007/BF02249755
4. Abdallah CG, Averill LA, Akiki TJ, Raza M, Averill CL, Gomaa H, et al. The neurobiology and pharmacotherapy of posttraumatic stress disorder. Annu Rev Pharmacol Toxicol. 2019;59:171–89.
5. Schrader C, Ross A. A Review of PTSD and Current Treatment Strategies. *Missouri medicine : journal of the Missouri State Medical Association*. 2021;118(6):546-551.
6. *CARDURA*. (1990). https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/019668Orig1s032lbl.pdf
7. Chung, M. S., Vashi, V., Puente, J. L. P., Sweeney, M., & Modesti, P. A. (1999). Clinical pharmacokinetics of doxazosin in a controlled-release gastrointestinal therapeutic system (GITS) formulation. *BJCP. British Journal of Clinical Pharmacology/British Journal of Clinical Pharmacology*, *48*(5), 678–687. https://doi.org/10.1046/j.1365-2125.1999.00067.x
8. Smith, C., & Koola, M. M. (2016). Evidence for using doxazosin in the treatment of posttraumatic stress disorder. *Psychiatric Annals*, *46*(9), 553–555. https://doi.org/10.3928/00485713-20160728-01