Prazosin for Posttraumatic Stress Disorder/Trauma-Related Nightmares

Psychological Health Center of Excellence Psych Health Evidence Briefs

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Q. What is prazosin?
A. Prazosin is a noradrenaline alpha-blocker medication with Food and Drug Administration (FDA) approval for the treatment of hypertension to lower blood pressure (U.S. Food and Drug Administration, 2009). Prazosin is used off-label to treat anxiety, posttraumatic stress disorder (PTSD), and trauma-related nightmares.

Q. What are the potential mechanisms of action underlying prazosin?
A. Dysregulation of the adrenergic system was first identified as a contributing mechanism in PTSD decades ago (Kosten, Mason, Giller, Ostroff, & Harkness, 1987), and it is hypothesized that dysregulation of noradrenergic neurons is specifically associated with hyperarousal and re-experiencing symptoms (Southwick et al., 1997). Prazosin, an α1-adrenergic receptor antagonist, is thought to counteract the noradrenergic hyperactivity that results in the intrusive and hyperarousal symptoms characteristic of PTSD. Similarly, α1-adrenergic receptor stimulation is thought to contribute to sleep disruption and trauma nightmares (Boehnlein & Kinzie, 2007; Mellman, Kumar, Kulick-Bell, Kumar, & Nolan, 1995).

Q. Is prazosin recommended as a front-line treatment for PTSD/trauma-related nightmares in the Military Health System (MHS)?
A. No. The 2017 VA/DoD Clinical Practice Guideline (CPG) for the Management of Posttraumatic Stress Disorder and Acute Stress Disorder gives a “Weak Against” strength of recommendation for prazosin to treat global symptoms of PTSD, either as a monotherapy or augmentation therapy. In addition, the CPG states that there is insufficient evidence to recommend for or against the use of prazosin as a monotherapy or augmentation therapy for nightmares associated with PTSD.

The MHS relies on the VA/DoD CPGs to inform best clinical practices. The CPGs are developed under the purview of clinical experts and are derived through a transparent and systematic approach that includes, but is not limited to, systematic reviews of the literature on a given topic and development of recommendations using a graded system that takes into account the overall quality of the evidence and the magnitude of the net benefit of the recommendation. A further description of this process and CPGs on specific topics can be found on the VA clinical practice guidelines website.

Q. Do other authoritative reviews recommend prazosin as a front-line treatment for PTSD/trauma-related nightmares?
A. No. Other authoritative reviews have not substantiated the use of prazosin for PTSD/trauma-related nightmares.

Several other recognized organizations conduct systematic reviews and evidence syntheses on psychological health topics using similar grading systems as the VA/DoD CPGs. These include the Agency for Healthcare Research and Quality (AHRQ) and Cochrane.

- AHRQ: A 2018 systematic review update of psychological and pharmacological treatments for adults with PTSD found that prazosin reduced PTSD symptoms, but the strength of evidence was low (Forman-Hoffman et al., 2018).
- Cochrane: No systematic reviews evaluating prazosin as a treatment for PTSD/trauma-related nightmares were identified.

Q. Is there any recent research on prazosin as a treatment for PTSD/trauma-related nightmares?
A. A June 2018 literature search identified two randomized controlled trials (RCTs) published after the earlier literature search was conducted for the 2017 VA/DoD Clinical Practice Guideline for the Management of Posttraumatic Stress Disorder and Acute Stress Disorder. The first RCT was conducted with 32 veterans with war-related PTSD who were randomly assigned to received prazosin or a placebo for eight weeks (Khazaie, Nasouri, & Ghadami, 2016). There were no significant differences found between treatment
groups on PTSD symptoms or trauma-related nightmares. Although published in 2018, results from the second RCT were evaluated and taken into consideration for the 2017 VA/DoD Clinical Practice Guideline for the Management of Posttraumatic Stress Disorder and Acute Stress Disorder (Raskind et al., 2018).

Q. What conclusions can be drawn about the use of prazosin as a treatment for PTSD/trauma-related nightmares in the MHS?

A. Although results from early RCTs evaluating prazosin as a treatment for PTSD/trauma-related nightmares appeared promising (Germain et al., 2012; Raskind et al., 2003; Raskind et al., 2007; Raskind et al., 2013), these trials varied in quality, and a more recent, large, well-designed trial did not find prazosin to be efficacious for either PTSD symptoms or nightmares (Raskind et al., 2018). Thus, prazosin is not recommended as a front-line treatment for PTSD or trauma-related nightmares in the MHS.


References


