

# Doxazosin for the Treatment of Nightmares in Post-Traumatic Stress Disorder: A Scoping Review of Clinical Evidence

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## ABSTRACT

Post-traumatic stress disorder is a debilitating condition caused after exposure to a traumatic event. One of the most difficult symptoms to treat is nightmares and sleep disturbances. There are limited pharmacological treatment options, and all are off-label in most countries. Evidence suggests that hyperstimulation of  $\alpha_1$ -adrenergic receptors in the prefrontal cortex contributes to hyperarousal, trauma-related nightmares, and sleep disturbances. Over the past 30 years, patients with this condition have been treated mostly with the first-generation  $\alpha_1$ -adrenergic antagonist prazosin. Doxazosin, a third-generation  $\alpha_1$ -adrenergic blocker, has been less extensively studied for such symptoms. Embase, PubMed, Cochrane, Google Scholar, and clinicaltrials.gov were searched from 1995 to 2025 to identify studies that reported doxazosin treatment in adults with a clinical diagnosis of post-traumatic stress disorder and nightmares and/or sleep disturbances. Out of the 143 reviewed articles, a total of 8 studies were included in this review. Across all included studies, doxazosin demonstrated positive effects in the treatment of nightmares. The methodological strengths and limitations, as well as results and outcome measures for each study, are discussed. The aim of this scoping review is to map existing evidence, identify knowledge gaps, and assess if doxazosin can be an appropriate therapeutic option. Although evidence supporting doxazosin as a treatment for nightmares in post-traumatic stress disorder is promising, the current body of evidence is very limited. Further research is needed to support the efficacy of doxazosin in diverse patient populations.

**Keywords:** Doxazosin, nightmares, PTSD, scoping review, treatment

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## INTRODUCTION

Post-traumatic stress disorder (PTSD) is an enduring and disabling condition secondary to exposure to traumatic events. According to the eleventh edition of the International Classification of Diseases, PTSD is defined as “a delayed or prolonged response to an exceptionally threatening or catastrophic event or situation, in which the individual’s reaction involves intense fear, helplessness, or horror.” The World Health Organization estimates that over 3.9% of the population suffers from PTSD. Although over 70% of the population is exposed to traumatic events, only 5.6% goes on to develop PTSD within

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1-3 months of exposure to a traumatic event. Post-traumatic stress disorder rates are higher in war-related traumas and sexual violence. Rates up to 70% have been reported in refugees and war survivors. Post-traumatic stress disorder incidence after sexual assault/rape ranges between 40% and 60%, and it is worse for men. Lifetime prevalence can be up to 9.6%. Natural disasters are less likely to result in persistent PTSD. About 40% of patients may recover within a year, but only 1 in 4 seek professional help.<sup>1</sup> Prevalence in older adults is estimated to be between 1.5% and 4%, and they are reported to be at higher risks of developing cognitive impairment and dementia.<sup>2</sup>

Among the core symptoms of PTSD are re-experiencing the index traumatic event, flashbacks, avoidance of places or situations associated with the trauma, hyperarousal, sleep disturbances, and nightmares. This can lead to anxiety, depression, mood lability, cognitive decline, and self-destructive tendencies. The prevalence of addiction to opioids, benzodiazepines, and alcohol in PTSD sufferers is 3-4 times higher than the general population.<sup>3</sup>

The pathophysiology of PTSD is thought to be a complex interaction of psychological, neurobiological, and epigenetic factors. Brain structures involved are the amygdala, hippocampus, and the prefrontal cortex. Neurotransmitter networks known to be affected are the noradrenergic system (hyperarousal and increased stress responses), serotonin, dopamine, and the hypothalamic-pituitary-adrenal axis.<sup>4</sup>

The pharmacogenomics of PTSD are multi-factorial, and some gene variants predispose individuals to a higher risk of developing PTSD. The *FKBP5* and *CRF-1/2* (encode receptors) genes are involved in the stress response. Specific variants increase PTSD risk and response to selective serotonin reuptake inhibitor (SSRI) treatments. Individuals with these genetic variations who develop PTSD when exposed to trauma are more likely to develop an addiction to cocaine and alcohol.<sup>5</sup>

Nightmares are of particular interest in all trauma- and stressor-related disorders because they are reported to be frequent, recurring, and can persist for several years. The prevalence of nightmares in PTSD specifically can be up to 96%. More than 50% of patients report trauma-related nightmares on a nightly basis.<sup>6</sup> Such symptoms can be severe and resistant to psychotherapeutic trauma-focused therapies as well as pharmacological treatments. As a result, there can be significant impairment in daytime functioning and psychological well-being. Post-traumatic stress disorder patients have been known to avoid sleep because of nightmares. Lack of sleep can result in hallucinations, psychotic behaviors, and in severe cases, uncontrolled addiction, deliberate self-harm, and suicide.<sup>7</sup>

Treatments for PTSD-related sleep disturbances and nightmares are mainly psychotherapeutic and include cognitive behavioral therapy, exposure therapy, eye movement desensitization and reprocessing, imagery rehearsal therapy, and exposure, relaxation, rescripting therapy, along with other trauma-focused therapies.<sup>8</sup> There are no licensed pharmacological treatments for the treatment of nightmares and sleep disturbances for PTSD patients specifically.<sup>9</sup> This poses a significant roadblock in treating those patients in specialist care.

The Food and Drug Administration in the USA and the Medicines and Healthcare Products Regulatory Agency in the UK have approved SSRIs such as sertraline and paroxetine for the treatment of PTSD. In Chinese medicine, PTSD is treated with Kaixinsan powder.<sup>10</sup>

Numerous studies report that patients are treated with a variety of antidepressants, antipsychotics, mood stabilizers, cannabinoids, antihistamines, benzodiazepines, and hypnotics that are all off-label, due to SSRI treatment failure.<sup>11</sup>

It is estimated that a mere 20%-30% of patients achieve PTSD remission with current treatments, if at all.<sup>12</sup> In addition to addiction problems, PTSD patients have been reported to suffer from chronic pain. The prevalence of chronic pain is high in these patients and can amount to 93%.<sup>13</sup>

Prazosin, a quinazoline derivative, is a first-generation postsynaptic alpha-1 adrenoreceptor antagonist that has been shown to improve nightmares in PTSD patients (off-label). Prazosin is the most extensively studied and prescribed  $\alpha$ 1-blocker for nightmares and sleep disturbances in PTSD patients. It has been shown to improve sleep quality and reduce sleep discontinuity, excessive dreaming, and nightmares. It is mostly well tolerated in both adults and children, with the most frequent side effects being orthostatic hypotension, dizziness, syncope, and daytime sedation. It can have a significant first-dose effect, resulting in fast-onset hypotension.<sup>14</sup> Patients on prazosin have reported breakthrough nightmares in the middle of the night as the dose wears off. As it has a short half-life of 2-3 hours, it requires frequent dosing—up to 4 times a day—in order to be effective. Higher daily doses are generally required for a therapeutic effect. This may lead to compliance issues and therapeutic failure, especially if hyperarousal symptoms persist during the day or if the blood pressure becomes too low. Doses range from 0.5  $\mu$ g to 12 mg daily. Slow titration and close monitoring are recommended.<sup>15,16</sup>

Doxazosin, a third-generation  $\alpha$ 1-adrenergic blocker (quinazoline derivative), was developed in 1977 and marketed in 1990. It is used for hypertension, benign prostatic hyperplasia, and PTSD-related nightmares. The extended-release (XL) formulation requires no titration, and dosing is once daily. A starting dose of 4 mg per day can be effective for PTSD-related nightmares. Compared to prazosin, it has a longer half-life of 22 hours and fewer blood pressure fluctuations. As a result, doxazosin has a better side-effect profile and better compliance compared to prazosin.<sup>17</sup>

There are not any large randomized controlled trials (RCTs) exploring the efficacy of doxazosin for PTSD-related nightmares. The majority of evidence discusses prazosin and psychosocial interventions.<sup>18-21</sup>

In a recent systematic review and meta-analysis by Skeie-Larsen et al<sup>22</sup> (2022) discussing treatments for PTSD nightmares, there was a reference to doxazosin but no evidence for comparison. The study reported that prazosin had a moderate effect size, with nabilone and hydroxyzine performing better, but there were not enough RCTs with the latter to increase confidence in those results.<sup>22</sup>

A recent study by Norred et al<sup>23</sup> (2024) discussed new and upcoming treatments for PTSD-related sleep disturbances and nightmares, with novel pharmacological treatments targeting the pharmacogenomics of PTSD. Doxazosin was discussed as a treatment, and the lack of enough clinical trials was also highlighted.<sup>23</sup>

Our findings indicate that from 1995 until now, the only drug therapy for PTSD-related nightmares consistently researched is prazosin. There was only 1 published pilot clinical trial with doxazosin XL by Rodgman et al<sup>24</sup> in 2016. One more clinical trial about doxazosin

was identified in clinicaltrials.gov, trial NCT03339258, in the US, that ended in 2024. Results are yet to be made available.<sup>25</sup>

The primary objective of this scoping review is to map practices and research doxazosin's use and efficacy in clinical practice, for PTSD-related nightmares, as well as identify any knowledge gaps in this area. Findings suggest that there are numerous knowledge gaps, non-standardization of doses, treatment durations, and outcome measures in clinical practice. There is limited information about the pharmacogenetics of doxazosin and why it works for some PTSD patients. Furthermore, there is a distinct lack of RCTs and clinical evidence base.

## MATERIAL AND METHODS

### Search Strategy and Study Selection

PubMed, Embase, Google Scholar, Cochrane Library, and clinicaltrials.gov were searched in order to identify articles about the treatment of PTSD-related nightmares and sleep disturbances with doxazosin for PTSD from 1990 until 2025.

Keywords used across all databases were "doxazosin" AND "Post-Traumatic Stress Disorder" OR "PTSD" AND/OR "nightmares."

The initial search for PTSD and nightmares produced 43 systematic reviews, 64 RCTs, and 19 meta-analyses of interest. The second search for PTSD and doxazosin produced 19 results.

One RCT discussing doxazosin for PTSD and alcohol in veterans by Back et al<sup>26</sup> (2023) was not included as it did not meet the criteria. The search in Cochrane library produced only 3 results and none were related to doxazosin. From the other databases, 1 pilot RCT was identified for doxazosin that met inclusion criteria and 1 RCT in clinicaltrials.gov that has not published any findings.

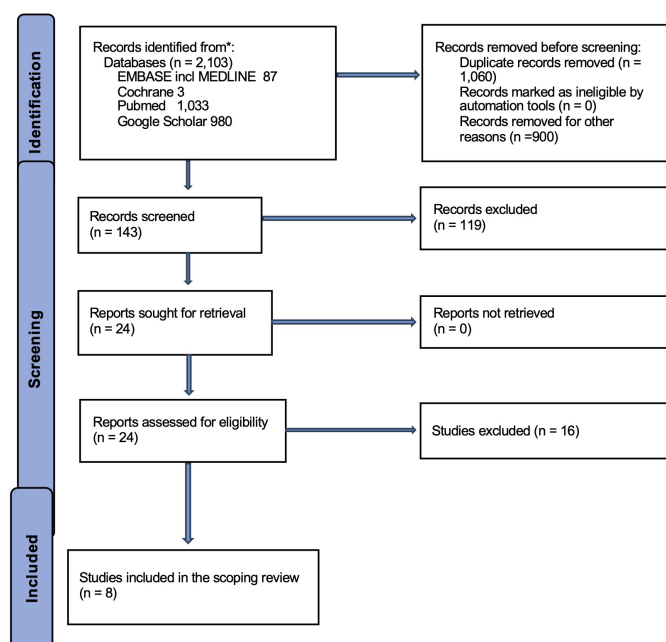
Inclusion criteria were randomized clinical trials, open clinical trials, observational studies, and case reports, in English, for adults, that reported the use of doxazosin in PTSD-related nightmares and sleep problems. Exclusion criteria were studies that did not review nightmares or sleep disturbances as outcomes in PTSD following treatment with doxazosin. Out of the 2103 articles across all databases, after duplicates and articles that were not relevant to the scope of this review were removed, a total of 143 articles were selected for screening. Authors screened articles independently, and studies were included if all agreed.

After screening titles and abstracts, a total of 24 articles were selected. Out of those, 11 articles were chosen for full-text review. From those 11 articles, 3 articles were excluded that were discussing the merits of doxazosin but did not include any patient data or outcome measures, resulting in 8 articles for inclusion in this review. The PRISMA flowchart showing study selection can be seen in Figure 1. Due to the very limited amount of evidence in the literature, the number of included studies was small.

### Quality of Evidence

The RCT risk of bias was assessed with the risk of bias tool version 2 (RoB-2).<sup>27</sup> The non-RCTs were assessed with the ROBINS-I V2 tool.<sup>28</sup>

The funnel plot in Figure 1 shows Egger's regression test, assessing publication bias for included studies. The risk of bias classifications can be seen in Table 1 for each study.



**Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart of included studies for this scoping review.**

## RESULTS

This scoping review discusses 8 articles in total that are summarised in Table 1. Included studies consist of 1 RCT, 2 open-label pilot studies, 1 retrospective chart review, 2 case series, and 2 case reports. In Figure 2, a visual representation of the publication bias for included studies can be seen.

Rodgman et al<sup>24</sup> (2016) in a pilot RCT, studied the efficacy of doxazosin XL in PTSD. Eight male combat veterans (mean age 34.8 years) with a confirmed DSM-IV (Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition) (PTSD diagnosis) were enrolled. The first part of the study involved treatment with doxazosin XL and the second, treatment with placebo. Over 16 days doxazosin XL was titrated from 4 mg/day to 16 mg/day. Outcomes were measured using the PTSD checklist–military version (PCL-M) and the Clinician-Administered PTSD Scale (CAPS-17). There were insignificant differences in the beginning and ending overall CAPS-17 scores. A general reduction in the CAPS hyperarousal subscale ( $P < .10$ ) was reported during the doxazosin XL phase. Self-reported PTSD symptom severity showed statistically significant improvement, supported by PCL-M scores ( $P = .002$ ).

De Jong et al<sup>35</sup> (2010) conducted a 4-week doxazosin XL variable dose open-label study with 12 participants with a diagnosis of PTSD and severe sleep disturbances. There were 4 males and 8 females, mean age  $37.9 \pm 9$  years. The study reported a significant reduction in the total score for the CAPS scale from 77 at the beginning of the trial to  $72 \pm 8$  at the end. Scores decreased to  $55 \pm 22$  at 8 weeks ( $P = .006$ ) and  $53 \pm 18$  at 12 weeks ( $P = .005$ ). Scales evaluating recurrent nightmares and difficulties in falling or staying asleep showed improvement, as they declined from  $13.4 \pm 1.6$  at baseline to  $8.8 \pm 4.5$  at 12 weeks ( $P = .012$ ). There were no clinically significant variations in blood pressure or heart rate. Doxazosin XL was generally well tolerated and showed overall good therapeutic

Table 1. Included Studies

Author, Year	Study Type	Sample	Intervention	Outcome Measures	Main Findings	Risk of Bias
Rodgman et al, 2016 <sup>24</sup>	RCT	8 veterans with PTSD	Doxazosin XL 4-16 mg/day, 16 days	CAPS-17, PCL-M	Trend towards reduced hyperarousal (CAPS) and significant reduction in PCL-M	Moderate
De Jong et al, 2010 <sup>35</sup>	Open-label pilot study	12 patients with PTSD (4 men, 8 women)	Doxazosin XL 4 mg, titrated to 8 mg in 8 weeks	CAPS, sleep assessment	Significant reduction in CAPS and nightmares ( $P=.012$ ), with mild adverse effects	Moderate
Richards et al, 2018 <sup>36</sup>	Open-label pilot study	15 adults with PTSD (8 completed)	Doxazosin XL 4-8mg in 8 weeks	CAPS, PCL, PSQI, sleep diary	Improvement in PTSD and sleep quality, but high dropout rate due to adverse effects	Low
Roepke et al, 2017 <sup>37</sup>	Retrospective chart review	51 patients with PTSD and/or BPD	Doxazosin XL (individualized dose, mean 6.08 mg/day)	CAPS B2	Significant reduction in CAPS B2, 25.8% achieved complete remission of nightmares	Low
Calegario et al, 2019 <sup>38</sup>	Case series	3 patients with PTSD and MDD	Doxazosin 1-4 mg/day based on response	Clinical assessment, patient reports	Doxazosin improved nightmares in all cases	Low
Khan et al, 2024 <sup>39</sup>	Case series	3 patients with PTSD, previously on prazosin	Doxazosin IR 1-8 mg/day based on tolerance	Clinical assessment, long-term follow-up	Replacement of prazosin with doxazosin IR maintained symptom remission	High
Sethi & Vasudeva, 2012 <sup>40</sup>	Case report	1 veteran with PTSD, hypertension, and BPH	Doxazosin 1-4 mg/day	PTSD checklist (military version)	Improvement in nightmares and intrusive memories with good tolerability	Moderate
Pallesen et al, 2020 <sup>41</sup>	Case report	1 patient with PTSD (56 years old)	Doxazosin 0-8 mg/day, sleep diary	Sleep diary, dose-response analysis	Dose-dependent reduction in nightmares, no tolerance to treatment	Moderate

BPD, borderline personality disorder; BPH, benign prostatic hyperplasia; CAPS-17, Clinician-Administered PTSD Scale; IR, immediate release; MDD, major depressive disorder; PCL-M, PTSD checklist–military version; PTSD, post-traumatic stress disorder; RCT, randomized controlled trial.

response, with some side effects. Two patients stopped the trial due to drowsiness (1 after 1 day and the other after 10 weeks), while 3 patients did not tolerate the 8 mg dose and continued at a reduced dose of 4 mg once daily. In an open-label, pilot study, Richards et al<sup>36</sup> (2018) evaluated the efficacy of doxazosin (XL) for treating nightmares, sleep disturbances, and overall PTSD symptoms. Eight out of the fifteen participants completed the trial over 8 weeks. Of those who dropped out, 4 participants stopped due to side effects and 3 due to other reasons. The CAPS mean total score decreased significantly from 57.3 at baseline to 31.5 at the end of the trial ( $z=2.52$ ,  $P=.012$ ). In addition, the CAPS subscale for distressing dreams showed a significant reduction—from 5.5 (SD=5.78) to 2.4 (SD=2.6) ( $z=2.49$ ,  $P=.013$ ). There was a non-statistically significant decrease in the overall CAPS sleep disturbance scores. Sleep diary data from all 11 participants showed a significant reduction in the frequency of nightmares ( $z=-2.8$ ,  $P=.006$ )

and enhanced subjective sleep quality (Skillings–Mack score=3.1,  $P=.014$ ) over the course of the trial.

A retrospective study by Roepke et al<sup>37</sup> (2017) reviewed the effectiveness of doxazosin XL treatment in PTSD-related nightmares in a sample of 51 patients. These patients had diagnoses of PTSD and/or comorbid borderline personality disorder (BPD). Study duration was 12 weeks. Patients were mostly female with a mean age of 35.7 years. Doxazosin XL dosing started at 1 mg at night and by the end of the study, the dose had increased by weekly increments to 8 mg/day. Nightmare severity was assessed with the CAPS-B2 scale which is specific to PTSD nightmares. A subgroup analysis of the PTSD subgroup showed symptom improvement—ANOVA, ( $F(2,36)=6.57$ ,  $P=.006$ ). At the end of 12 weeks, 25.8% of all patients reported complete remission of nightmares with a CAPS B2 score of 0.

A case series of 3 male patients by Calegario et al<sup>38</sup> (2019) reported findings in severe PTSD and comorbid major depressive disorder following low dose doxazosin XL treatment. The first patient had nightmares on average 3 times a week and was on venlafaxine 225 mg, quetiapine 125 mg, and chlorpromazine 200 mg daily. The patient responded well to doxazosin XL 4 mg/day and was nightmare-free at the 4 monthly follow-up. The second patient that had PTSD, type-2 diabetes, and hypercholesterolemia, responded well to 2 mg/day doxazosin, and his 2-a-weekly nightmares receded at 7 weeks. The patient was also on sertraline 200 mg, chlorpromazine 300 mg, and clonazepam 2 mg daily. The third patient responded well to a maintenance dose of doxazosin of 2 mg/day. While nightmares did not completely resolve, there was a very significant reduction in frequency to less than once a week. This patient was also on sertraline 200 mg, lithium carbonate 1500 mg, and clonazepam 1 mg daily. Khan et al<sup>39</sup> (2024) compared doxazosin immediate release with prazosin in a 3 patient case series. The first patient was a 72-year-old male with PTSD and other psychiatric

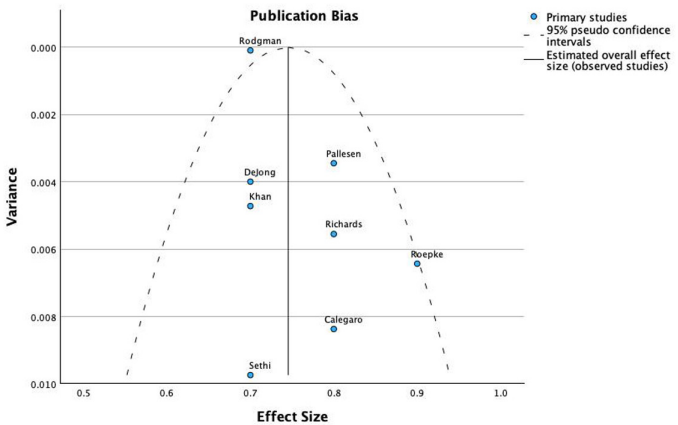


Figure 2. Scoping review included studies, publication bias, using Egger's regression test.



comorbidities—obsessive-compulsive disorder and schizoaffective disorder. That patient had previously responded well, reporting a 90% reduction in nightmares, with prazosin 6 mg/daily divided into 3 × 2 mg doses. The patient achieved full remission of nightmares and flashbacks with 4 mg doxazosin daily, that was maintained at follow-up at 26 months. The second patient, a 73-year-old female with long-term PTSD from childhood abuse, responded well to 8 mg/day of prazosin divided in 4 × 2 mg doses. That patient responded well to a maintenance dose of 8mg/day doxazosin and nightmares were in full remission at follow-up, after 20 months. The third patient, a 63-year-old female with PTSD secondary to sexual abuse, did not tolerate prazosin 1 mg twice daily as she experienced over-sedation. The patient responded well to 1 mg/day of doxazosin and nightmares receded significantly. In a case report by Sethi and Vasudeva<sup>40</sup> (2012), a 59-year-old male Vietnam veteran with PTSD, comorbid hypertension, and benign prostatic hyperplasia, reported a marked improvement in nightmare frequency and intensity following treatment with 4 mg/day doxazosin XL. Nightmares receded significantly, and sleep quality was improved after 8 weeks of treatment. The patient reported some side effects at the beginning of treatment—due to orthostatic hypotension—however those receded at 8 weeks. The patient had tried various other medications to address his PTSD sleep disturbances in the past with little effect. Pallesen et al<sup>41</sup> (2020) reported the case of a 56-year-old female PTSD patient, whose response to variable dose treatment was described in a diary-based study over 280 days. Results showed that the patient responded well to a maintenance dose of 8 mg/day doxazosin XL and had a significant reduction in nightmares, with some dizziness, a single episode of fainting and no significant overall variation in blood pressure.

## DISCUSSION

This scoping review identified a small but positive evidence base that suggests that doxazosin at the right dose can be an effective treatment for PTSD-related nightmares and sleep disturbances.

The study by De Jong et al<sup>35</sup> (2010) was interesting because it included a 4-week observation phase prior to the actual trial in order to exclude spontaneous symptom remission. The small sample size of 12 participants, the open-label design, and lack of placebo limit result generalizability. Doxazosin XL was mostly well tolerated, but patients reported adverse drug reactions at higher doses, such as drowsiness, and thus discontinued treatment. The study by Rodgman et al<sup>24</sup> (2016), although an RCT, has several limitations. This study has a small sample size of only 8 participants and includes only males who developed PTSD following military assignments. As such, results cannot be easily generalized to other patient populations who developed PTSD because of other reasons. Treatment duration was only 16 days, and it can be difficult to capture the full spectrum of treatment versus response over such a short time. However, the use of both CAPS-17 and self-report (PCL-M) scales gives valuable insights into the response to treatment over time, albeit short.

Sethi and Vasudeva<sup>40</sup> (2012) discussed the case of a treatment-resistant PTSD patient. Results were reported using a military version of a PTSD checklist. It can be difficult to conclude the effectiveness of doxazosin from this individual case, as the patient's prior treatment resistance could be attributed to individual genetic variation or other unknown confounding variables. The case series by Calegario et al<sup>38</sup> (2019) and Khan et al<sup>39</sup> (2024) lack statistical power, as they

report individual patient cases with other mixed comorbidities and polypharmacy. There are not any standardized reporting scales, and as such, it is difficult to ascertain the effectiveness of doxazosin treatment beyond these cases. There were not any control groups, and doxazosin dosing was adapted for each patient, based on tolerability and side effects. Furthermore, follow-up was not consistent. Therefore, these results cannot be generalized to other PTSD patient populations. In addition, doxazosin serum levels were not measured in those cases; therefore, it can be difficult to identify a mean effective treatment dose.

Roepke et al<sup>37</sup> (2017), in their 12-week retrospective chart review of patients with PTSD and PTSD with BPD, used the CAPS B2 to assess PTSD nightmares. The study included female civilian patients, which addressed a literature gap, as there is a lack of such studies. The limitations of this study include the study design, as it allows for selection bias, and it assumes that chart data are accurate. In addition, doxazosin XL dosing was not uniformly controlled, as it was individually adapted for each patient, based on tolerability and dose-response to treatment. Richards et al<sup>36</sup> (2018), in their open-label trial over 8 weeks, used the CAPS scale and various other self-report instruments such as the Pittsburgh Sleep Quality Index and the PTSD checklist for DSM-5, as well as daily sleep diaries. The patient population was mixed, as it included both complex PTSD and PTSD patients. The sample size was small. There was a comprehensive all-round assessment strategy that reported significant improvement in PTSD-related nightmares and other overall symptoms. However, there was a relatively high dropout rate of 27%, which was reported to be secondary to doxazosin's side effects.

The 280-day diary-based case report by Pallesen et al<sup>41</sup> (2020) reinforced reports from previous cases that there is a close dose-response relationship for PTSD patients treated with doxazosin XL. It can be difficult to generalize results about the efficacy of doxazosin from this case alone, however. In this study, time was designated as a confounding factor in an elaborate logistic regression statistical analysis, something that was not considered in previously published cases. Findings suggest that individualized doxazosin XL dosing, based on treatment response and accounting for any side effects, is more likely to achieve good therapeutic results.

Doxazosin has more advantages than prazosin. It can be taken at any time during the day due to the long half-life of 22-30 hours. Prazosin must be taken 3-4 times a day, as it has a half-life of 2-3 hours. Doxazosin is not subject to the first-dose hypotensive effect that prazosin is, and due to its pharmacokinetic and pharmacodynamic profile and better absorption, it lowers blood pressure in a steady controlled manner. Prazosin has been reported to run out during sleep, and patients have breakthrough nightmares. Higher doses are required to reach the therapeutic effect. Doxazosin XL can be started at 4 mg daily without the need for titration. Prazosin needs to be started at doses of 0.5 µg, and requires careful and gradual titration to avoid abrupt blood pressure changes and sedation. Treatment compliance is higher with doxazosin XL compared to prazosin.

Doxazosin is currently in phase 2 testing for treating PTSD symptomatology.<sup>29</sup>

Studies assessing the effectiveness of both prazosin and doxazosin in patients with comorbid PTSD and alcohol use disorder (AUD) have been inconclusive.

Raskind et al<sup>30</sup> (2016) in an RCT assessing prazosin's effect on alcohol harm reduction in PTSD veterans, reported that prazosin could help in reducing alcohol consumption. Haass-Koffler et al<sup>31</sup> (2017) reported in an RCT assessing the effects on alcohol consumption in veterans with PTSD-AUD treated with doxazosin XL, that compared with prazosin it is more effective in reducing alcohol abuse in individuals with high-risk factors. Wilcox et al<sup>32</sup> (2018) in another RCT assessing prazosin's effect on alcohol consumption in PTSD-AUD patients, reported that prazosin was somehow effective, but poor compliance and tolerance may have affected outcomes. Back et al<sup>33</sup> (2023) in an RCT assessed doxazosin XL 16 mg over 16 days and its effect on alcohol consumption in veterans with PTSD-AUD. The study reported no difference in alcohol intake, but good overall tolerability and compliance.

Gully et al<sup>34</sup> (2023) advocate the use of MDMA (3,4-methylenedioxymethamphetamine, or else ecstasy) for PTSD-AUD and report other pharmacological treatments like doxazosin and prazosin as inconclusive.

There are few pharmacological options for the treatment of nightmares in PTSD patients. This scoping review identified a small but promising body of evidence supporting the efficacy and safety of doxazosin XL for the treatment of nightmares in PTSD. Doxazosin can be considered an alternative to prazosin when prazosin is not available or when patients do not tolerate it. While current evidence supports its potential benefits, randomized controlled trials with more diverse patient populations are necessary to confirm its long-term efficacy and inform clinical practice.

**Data Availability Statement:** The data that support the findings of this study are available from the corresponding author, SK, upon reasonable request.

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept – I.C.P.; Design – I.C.P.; Supervision – S.K.; Resources – I.C.P.; Materials – I.C.P.; Data Collection and/or Processing – I.C.P.; Analysis and/or Interpretation – S.K.; Literature Search – I.C.P.; Writing Manuscript – S.K.; Critical Review – S.K.

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