

Is there a role for prazosin in the treatment of post-traumatic stress disorder?

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This article is the next in our series of occasional papers 'At the cutting edge', where we invite researchers to inform readers on where they believe clinical practice is heading. The material published in this article is not mainstream or part of standard clinical practice. However, we hope readers will be inspired and enjoy contemplating where clinical medicine may lead in the future – the Editor.

Background

Post-traumatic stress disorder (PTSD) is a common disorder with significant morbidity and associated comorbidities, including mood disorders and substance abuse, and is frequently misdiagnosed or under-diagnosed. Management of PTSD requires combined psychotherapy and pharmacotherapy, but some symptoms, particularly nightmares and sleep disturbance, are often resistant to treatment.

Objective

The aim of this article is to inform primary healthcare professionals of the prevalence and significance of PTSD, and to review the evidence that prazosin is a useful option for managing PTSD-associated nightmares and sleep disturbance.

Discussion

PTSD should be considered in patients with treatment-resistant mood disorders. A trauma history should be taken for these patients and in recognised groups of patients who have a high incidence of PTSD. The treatment of PTSD is challenging, frequently requiring specialist input from psychiatrists. Prazosin has been proven to be safe and effective in the management of nightmares and sleep disturbances associated with PTSD and is indicated where these distressing symptoms are present.

Post-traumatic stress disorder (PTSD) is a common disorder, affecting 3–4% of the general population.¹ The incidence of PTSD is higher in certain groups including Aboriginal and Torres Strait Islander peoples,² people with substance abuse disorders,^{1,3} serving and ex-service military and emergency services personnel,¹ and prisoners.⁴

Detection of PTSD in primary care is clinically important. PTSD is a significant psychological disorder associated with increased morbidity, increased use of healthcare services, functional disability, increased suicide risk and premature death.⁵ Significant comorbidities include anxiety and depression,¹ tobacco smoking, alcohol and other substance abuse, poor diet and physical inactivity.^{1,5}

Diagnostic criteria and screening tools for PTSD

The diagnostic criteria for PTSD are specified in the fifth edition of the American Psychiatric Association *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5).⁶ The criteria are specific for adults and adolescents, and children older than 6 years. Diagnostic criteria for PTSD include a history of exposure to an actual or threatened traumatic event involving death, serious injury or sexual violation, which may be direct, witnessed or vicariously experienced if the trauma occurs to a close family member or friend. Symptoms from each of the four symptom clusters listed below must occur:

- intrusion
- avoidance
- negative alterations in cognitions and mood
- alterations in arousal and reactivity.

Other criteria concern duration of symptoms and impairment in important areas of functioning, and clarify that symptoms are not attributable to a substance or co-occurring medical condition.⁶

PTSD is frequently misdiagnosed or under-diagnosed.⁷ A useful screening tool is the Primary Care Post-Traumatic Stress Disorder Screen⁸ (Box 1). This screening tool can be supplemented by the PTSD checklist for DSM-5 (PCL 5)⁹ and structured diagnostic interviews such as the Clinician Administered PTSD Scale (CAPS), to confirm the diagnosis.¹⁰ CAPS should be reserved for use by health professionals with appropriate training in the delivery and interpretation of the scoring for this tool.

Initial approach to treatment of PTSD

PTSD is a difficult condition to treat and requires an integrated approach using disorder-specific psychological treatments such as trauma-focused cognitive behavioural therapy and eye movement desensitisation and reprocessing, and pharmacotherapy.^{11,12} In primary care, the recommended first-line pharmacotherapy agents for treating PTSD are selective serotonin reuptake inhibitors, such as paroxetine 20–40 mg once daily for at least 10 weeks. Second-line pharmacological interventions include the use of mirtazapine or phenelzine. It is recommended that only mental health professionals should initiate the use of

phenelzine. Where symptoms have not responded adequately, consideration should be given to increasing the dose of antidepressants (within approved limits), switching antidepressant or adding risperidone or olanzapine as an adjunct.¹¹

The role of prazosin in treating PTSD

Two significant distressing symptoms of PTSD, nightmares (intrusion) and sleep disturbance (alteration in arousal), are often resistant to pharmacological treatment.¹³ The mechanism for these symptoms appears to be enhanced postsynaptic adrenoceptor responsiveness to central nervous system (CNS) noradrenaline.¹³ Randomised clinical trials provide evidence that the off-label use of prazosin, a brain-active alpha-1 adrenoceptor antagonist, is effective and safe in the treatment of nightmares and sleep disturbance associated with PTSD, and contributes to an improvement in overall clinical status without affecting blood pressure.^{13–16}

Introducing prazosin into the treatment of a patient with PTSD is guided by the ‘start low, go slow’ rule. The recommended starting dose to minimise the risk of adverse drug reactions (ADRs) is 1 mg before bed, increasing by 1 mg every 2–3 nights until a clinical response is obtained. Average doses of prazosin in the treatment of PTSD achieved daily doses of 19.6 mg for males and 8.7 mg for females,¹² although there are reports

of higher doses being used.¹⁷ Prazosin is well tolerated and common ADRs include dizziness (10%), headache (8%), drowsiness (8%), lack of energy (7%), weakness (7%), palpitations (5%) and nausea (5%). A significant potential ADR is ‘first-dose syncope’ (1%), which occurs with doses of 2 mg or higher. Treatment, therefore, should always commence at a dose of 1 mg.¹⁸

Summary

This article provides a review of a role for prazosin as safe and effective pharmacotherapy for the distressing symptoms of nightmares and sleep disturbance in patients with PTSD.¹³ The authors recommend that treating practitioners consider and screen for PTSD in patients who are unresponsive to treatment for diagnoses such as bipolar disorders, anxiety and depression. Patients with common conditions such as alcohol and substance abuse should be screened for PTSD. This condition should be actively considered as a critical diagnosis in all Aboriginal and Torres Strait Islander patients, serving and ex-service military and emergency personnel, and prisoners. Consultation with a psychiatrist is recommended when any or all of the following factors are present:^{11,12}

- diagnostic uncertainty
- comorbid conditions
- severe or complex PTSD and concern about patient safety
- treatment resistance requiring sophisticated pharmacological strategies.

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Box 1 Primary Care Post-Traumatic Stress Disorder Screen⁸

In your life, have you ever had any experience that was so frightening, horrible or upsetting that, in the past month, you:

1. Have had nightmares about it or thought about it when you did not want to?	Yes	No
2. Tried hard not to think about it or went out of your way to avoid situations that reminded you of it?	Yes	No
3. Were constantly on guard, watchful, or easily startled?	Yes	No
4. Felt numb or detached from others, activities or your surroundings?	Yes	No

If a patient answers ‘YES’ to 2 or more questions, a diagnosis of PTSD is highly likely.

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