Indian Health Service
IHS National Pharmacy and Therapeutics Committee
Prazosin in Post-Traumatic Stress Disorder
February 2012

Background:

The IHS National Pharmacy and Therapeutics Committee (NPTC) reviewed the agents used in the management of anxiety disorders at their January 2012 meeting. The role of alpha$_1$ adrenergic antagonists in the management of Post-Traumatic Stress Disorder (PTSD) was reviewed. The NPTC **added** prazosin to the IHS National Core Formulary (NCF) due to its unique role in PTSD management. The committee did not feel that it was necessary to have all three non-selective alpha$_1$ adrenergic antagonists on the NCF. After a review of utilization data, the NPTC voted to **remove** terazosin from the NCF.

Discussion:

Post-traumatic stress disorder (PTSD) is one of several mental disorders classified as anxiety disorders. It is characterized by a history of exposure to trauma (actual or threatened death, serious injury, or threats to the physical integrity of the self or others) with a response of intense fear, helplessness or horror: with the later development of re-experiencing symptoms (intrusive recollections, flashbacks or dreams), avoidance symptoms (e.g., efforts to avoid activities or thoughts associated with the trauma), and hyper-arousal symptoms (including disturbed sleep, hypervigilance and an exaggerated startle response). The American Psychiatric Association (APA) guidelines recommend that selective serotonin reuptake inhibitors (SSRI) be used as first-line therapy for the management of PTSD, as these agents ameliorate all three PTSD symptom clusters (i.e., reexperiencing, avoidance/numbing, and hyperarousal)[1]. However, there is growing evidence for the use of alpha$_1$ adrenergic antagonist in the management of PTSD, particularly related to sleep disturbance and nightmares. PTSD has been associated with an increase in central nervous system adrenergic activity leading to an increased release of norepinephrine at receptor sites[2]. Increased activity occurs especially at night and has been associated with poor sleep and nightmares. Most studies have evaluated prazosin's role in reducing these symptoms, as it is the only alpha$_1$ adrenergic antagonist that crosses the blood-brain barrier. However, there is some limited data showing positive effects for the peripherally-acting agents, terazosin and doxazosin.

In 2003, Raskind et. al. reported on a 20-week double-blind cross-over study of prazosin vs. placebo in 10 Vietnam combat veterans with chronic PTSD and severe trauma-related nightmares. The mean dose of prazosin utilized was 9.5 mg/day given at bedtime. This regimen was proven superior to placebo related to decreasing the number of distressing nightmares, reducing the difficulty in falling and staying asleep, reduction in the overall PTSD severity and in symptom scores for all three PTSD symptom clusters[3].

In 2007, Raskind et. al. conducted a larger randomized controlled trial of 40 veterans with chronic PTSD and distressing trauma-related nightmares and sleep disturbances using a mean dose of 13.3 mg of prazosin vs. placebo for 8 weeks, confirming the reductions in distressing nightmares and improved sleep quality[4].

Taylor et. al published a randomized, placebo-controlled crossover trial in 2008 comparing prazosin vs. placebo in 13 civilian outpatients with chronic PTSD, frequent nightmares, and sleep disturbance using a mean dose of 3.1 mg of prazosin. This trial showed a reduction in nightmares accompanied by an increase in total sleep time, REM sleep time, and mean REM period duration without sedative-like effects on sleep onset latency[5].

A head-to-head trial comparing prazosin to quetiapine showed similar short-term efficacy in symptomatic improvement in PTSD. However, adverse effects were greater (34.9% vs. 17.7%; P=0.008) and continuation rates were lower (24% vs. 48.4%; P= 0.54) for the quetiapine group[6].

Findings:

The IHS NPTC believes good evidence exists for the use of prazosin in the treatment of PTSD, particularly cases where nightmares and sleep disturbance play a key role or where patients have failed first-line therapy with SSRIs. This formulary brief is intended to increase awareness among clinicians about this important therapeutic option.

If you have any questions regarding this document, please contact the NPTC at nptc1@ihs.gov.

References:

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