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References
8. van der Kolk BA: The Trauma Center Assessment Package. Brookline, Mass, Trauma Center, 1997

Brief Report

Reduction of Nightmares and Other PTSD Symptoms in Combat Veterans by Prazosin: A Placebo-Controlled Study

Murray A. Raskind, M.D.
Elaine R. Peskind, M.D.
Evan D. Kanter, M.D.
Eric C. Petrie, M.D.
Allen Radant, M.D.
Charles E. Thompson, M.D.
Dorcas J. Dobie, M.D.
David Hoff, PA-C
Rebekah J. Rein, J.D.
Kristy Straits-Tröster, Ph.D.
Ronald G. Thomas, Ph.D.
Miles M. McFall, Ph.D.

Objective: Prazosin is a centrally active α₁ adrenergic antagonist. The authors’ goal was to evaluate prazosin efficacy for nightmares, sleep disturbance, and overall posttraumatic stress disorder (PTSD) in combat veterans.

Method: Ten Vietnam combat veterans with chronic PTSD and severe trauma-related nightmares each received prazosin and placebo in a 20-week double-blind crossover protocol.

Results: Prazosin (mean dose=9.5 mg/day at bedtime, SD=0.5) was superior to placebo for the three primary outcome measures: scores on the 1) recurrent distressing dreams item and the 2) difficulty falling/staying asleep item of the Clinician-Administered PTSD Scale and 3) change in overall PTSD severity and functional status according to the Clinical Global Impression of change. Total score and symptom cluster scores for reexperiencing, avoidance/numbing, and hyperarousal on the Clinician-Administered PTSD Scale also were significantly more improved in the prazosin condition, and prazosin was well tolerated.

Conclusions: These data support the efficacy of prazosin for nightmares, sleep disturbance, and other PTSD symptoms.

Prazosin substantially reduced trauma-related nightmares and globally rated severity of posttraumatic stress disorder (PTSD) in open-label studies (1–3). Prazosin is a centrally active α₁ adrenergic antagonist long available for treating hypertension (4) that should counteract in part the excessive brain noradrenergic activity reported in PTSD (5).

Method
Ten male Vietnam combat veteran outpatients (mean age=53 years, SD=3) provided signed informed consent for participation in this study, which was approved by the University of Washington institutional review board. All of the patients met DSM-IV criteria for PTSD and had experienced PTSD symptoms since their return from Vietnam at least 25 years earlier. Five patients met criteria for alcohol abuse in the past, but all had been free of alcohol or other substance abuse for at least 6 months. All had frequent and severe combat-trauma-related nightmares, as defined by a score of 6 or higher on the Clinician-Administered PTSD Scale (6) recurrent distressing dreams item (maximum score=8), despite trials of psychoactive medications. Nine were receiving disability compensation for PTSD. Seven were receiving one or more of the following medications for PTSD: selective serotonin

TABLE 1. Effect of Crossover Treatment With Prazosin and Placebo on Symptom Measures for 10 Combat Veterans With Chronic PTSD

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>Pranzosin</th>
<th>Placebo</th>
<th>Analysis of Change Scores</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinician-Administered PTSD Scale</td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
</tr>
<tr>
<td>Recurrent distressing dreams</td>
<td>6.9</td>
<td>0.9</td>
<td>7.1</td>
</tr>
<tr>
<td>Endpoint</td>
<td>3.6</td>
<td>2.8</td>
<td>6.7</td>
</tr>
<tr>
<td>Difficulty falling/staying asleep</td>
<td>7.4</td>
<td>1.3</td>
<td>7.3</td>
</tr>
<tr>
<td>Endpoint</td>
<td>4.0</td>
<td>2.3</td>
<td>7.1</td>
</tr>
<tr>
<td>Total score</td>
<td>79.1</td>
<td>17.0</td>
<td>83.6</td>
</tr>
<tr>
<td>Endpoint</td>
<td>57.3</td>
<td>32.3</td>
<td>86.5</td>
</tr>
<tr>
<td>Reexperiencing/intrusion</td>
<td>23.1</td>
<td>6.6</td>
<td>23.7</td>
</tr>
<tr>
<td>Endpoint</td>
<td>17.0</td>
<td>11.4</td>
<td>24.0</td>
</tr>
<tr>
<td>Avoidance/numbing</td>
<td>33.0</td>
<td>7.7</td>
<td>30.6</td>
</tr>
<tr>
<td>Endpoint</td>
<td>26.6</td>
<td>15.9</td>
<td>35.0</td>
</tr>
<tr>
<td>Hyperarousal</td>
<td>29.9</td>
<td>5.4</td>
<td>29.3</td>
</tr>
<tr>
<td>Endpoint</td>
<td>20.6</td>
<td>9.1</td>
<td>27.4</td>
</tr>
<tr>
<td>Clinical Global Impression of change$^a$ (overall PTSD severity and function) at endpoint</td>
<td>2.0</td>
<td>0.5</td>
<td>4.5</td>
</tr>
</tbody>
</table>

$^a$1=markedly improved, 2=moderately improved, 3=minimally improved, 4=unchanged, 5=minimally worse, 6=moderately worse, 7=markedly worse.
astolic was 89 mm Hg (SD=8) supine and 84 mm Hg (SD=15) standing.

All patients completed all conditions except for those in the second placebo condition. Five patients experienced a rapid return of distressing nightmares during postprazosin washout. Four experienced no benefit from their second placebo treatment and insisted on discontinuing the study so they could be given open-label prazosin; these patients rapidly improved after receiving the active drug. Last observation carried forward analysis was selected to impute conservative endpoint 2 values for these subjects. Empirically, the change scores for these early termination patients were very similar to those for the five first-period placebo subjects.

Discussion

PTSD nightmares appear to arise from light sleep and/or disrupted REM sleep (11). Prazosin reduces light sleep and normalizes REM sleep (12). Prazosin reduces secretion of corticotropin-releasing hormone (13), a neuropeptide elevated in PTSD (14). The high CNS noradrenergic outflow in PTSD (5) likely stimulates α1 adrenergic regulation of the prefrontal cerebral cortex, disrupting cognitive processing and increasing fear responses (15). This is corrected by prazosin (15).

These results support the efficacy and safety of prazosin for trauma-related nightmares, sleep disturbance, and overall PTSD severity and function in previously treatment-resistant combat veterans. Prazosin offers a novel and inexpensive approach to nightmare reduction and other PTSD symptom relief for combat veterans. Further studies are necessary to replicate these findings and to determine if prazosin is effective in civilian trauma PTSD.

References


Received Feb. 5, 2002; revision received June 25, 2002; accepted July 28, 2002. From the Northwest Network VISN 20 Mental Illness Research, Education, and Clinical Center, VA Puget Sound Health Care System; the Department of Psychiatry and Behavioral Sciences, University of Washington, Seattle; and the Division of Biostatistics, Department of Family Medicine and Neurosciences, University of Washington, Seattle; and the Division of Biostatistics, Department of Family Medicine and Neurosciences, University of California, San Diego. Address reprint requests to Dr. Raskind, VA Puget Sound Health Care System (116 MIRECC), 1660 S. Columbian Way, Seattle, WA 98108; murray.raskind@med.va.gov (e-mail).

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