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TITLE: A Placebo-Controlled Trial of Prazosin vs. Paroxetine in Combat Stress-Induced PTSD Nightmares and Sleep Disturbance

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14. ABSTRACT The primary goal of this proposal is to evaluate the efficacy and tolerability of the alpha-1 adrenergic antagonist prazosin compared to placebo for combat trauma-related nightmares, sleep disturbance and overall function in recently combat-exposed returnees from OIF and OEF. A secondary goal is to evaluate the effects of the SSRI paroxetine on behavioral symptoms and overall function in this population. Specific hypotheses (described below) will be tested in a three parallel arm 12-week randomized controlled trial of prazosin, paroxetine and placebo in combat-exposed troops recently returned from OIF and OEF with combat trauma-related persistent nightmares and sleep disturbance. This will be a two-site study performed in the Seattle/Tacoma area at Madigan AMC and in the Washington DC area at Walter Reed AMC.					
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Introduction

The primary goal of this proposal is to evaluate the efficacy and tolerability of the alpha-1 adrenergic antagonist prazosin compared to placebo for combat trauma-related nightmares, sleep disturbance and overall function in recently combat-exposed returnees from OIF and OEF. A secondary goal is to evaluate the effects of the SSRI paroxetine on behavioral symptoms and overall function in this population. Specific hypotheses (described below) will be tested in a three parallel arm 12-week randomized controlled trial of prazosin, paroxetine and placebo in combat-exposed troops recently returned from OIF and OEF with combat trauma-related persistent nightmares and sleep disturbance. This will be a two-site study performed in the Seattle/Tacoma area at Madigan AMC and in the Washington DC area at Walter Reed AMC.

Body

IRB approvals - All study procedures and the consent forms have been approved by both the IRBs of Madigan Army Medical Center (AMC) and Walter Reed AMC. The current approval period for Madigan is 6/27/08-6/19/09. The current approval period for Walter Reed is 1/9/08-1/10/09.

Hiring/training of study personnel - all study personnel at VA Puget Sound Health Care System for performing all clinical study tasks at Madigan AMC and coordination, data management, and statistical analysis for both Madigan AMC and Walter Reed AMC have been hired and are on site. Training and certification for staff performing study activities at Madigan AMC was completed June 1, 2006. Hiring of personnel at the Walter Reed AMC site has been completed. The Seattle team conducted a study initiation visit at Walter Reed AMC in 11/06; final training and certification of staff at WRAMC was completed February 1, 2007.

Recruitment and enrollment of study subjects

Subject enrollment to date at each study are as follows:

Madigan AMC

- 189 subjects telephone prescreened
- 98 subjects consented
- 76 subjects randomized to treatment
- 22 study completers

Walter Reed AMC

- 108 subjects referred
- 72 subjects telephone prescreened
- 13 subjects consented
- 9 subjects randomized to treatment
- 6 study completers

Recruitment and retention remain a challenge in this participant population. Drs. Raskind and Peskind have made presentations to MAMC and WRAMC Behavioral Health, Primary Care, and Rehabilitation Medicine clinicians to inform them about study initiation and procedures for referral of potential participants prior to the opening of study enrollment. The Madigan AMC team attend SRPs and perform outreach activities to local Guard and Reserve units to provide

information re: study participation. Dr. Raskind developed collaboration with combat command personnel at Madigan AMC to intensify recruitment and retention activities. The Walter Reed AMC study team has undertaken extensive outreach to multiple primary care and speciality clinics to present training on posttraumatic stress disorder and specific information on this study to potential referral sources. Advertising and outreach for study recruitment, and participant retention activities are continuing.

Completion of clinical trial procedures – Screening and baseline assessments, repeat assessments, and follow-up, and completion of case report forms are ongoing.

Data monitoring and database management - Construction of the database was completed August 1, 2006. Data entry and data cleaning are continuous. Following completion of data cleaning, the database will be frozen. The Data Safety and Monitoring Board met for their second meeting very recently and their report is pending.

Statistical analysis and preparation of manuscripts and reports – Within 2 months of completion of data cleaning and freezing of the database, statistical analysis will be completed and initial manuscripts will be prepared. Additional manuscripts describing results of secondary analyses will be prepared thereafter.

Key Research Accomplishments - pending completion of data collection per above described timetable.

Research Findings – see above.

Conclusions - see above.

References – none.

Appendices – none.