Contemporary Clinical Trials 72 (2018) 126–136

Contents lists available at ScienceDirect

Contemporary Clinical Trials

journal homepage: www.elsevier.com/locate/conclintrial

Intensive prolonged exposure therapy for combat-related posttraumatic stress disorder: Design and methodology of a randomized clinical trial

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ARTICLE INFO

Keywords:
Posttraumatic stress disorder
PTSD
Prolonged exposure therapy
Intensive outpatient program
Military
Veterans

ABSTRACT

Combat-related posttraumatic stress disorder (PTSD) is the most common psychological health condition in military service members and veterans who have deployed to the combat theater since September 11, 2001. One of the highest research priorities for the Department of Defense and the Department of Veterans Affairs is to develop and evaluate the most efficient and efficacious treatments possible for combat-related PTSD. However, the treatment of combat-related PTSD in military service members and veterans has been significantly more challenging than the treatment of PTSD in civilians. Randomized clinical trials have demonstrated large post-treatment effect sizes for PTSD in civilian populations. However, recent randomized clinical trials of service

Abbreviations: CAP, Consortium to Alleviate PTSD; CAPS-5, Clinician-Administered PTSD Scale for *DSM-5*; CPT, cognitive processing therapy; DoD, U.S. Department of Defense; DSI-SS, Depressive Symptoms Index – Suicidality Subscale; *DSM-5*, Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition; IOP, intensive outpatient program; OEF, Operation Enduring Freedom; OIF, Operation Iraqi Freedom; OND, Operation New Dawn; PCL-5, PTSD Checklist for *DSM-5*; PE, prolonged exposure; PHQ-9, Patient Health Questionnaire-9; PTCI, Posttraumatic Cognitions Inventory; PTSD, posttraumatic stress disorder; RCT, randomized clinical trial; SUDS, Subjective Units of Distress Scale; TBI, traumatic brain injury; U.S., United States; VA, U.S. Department of Veterans Affairs.

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https://doi.org/10.1016/j.cct.2018.07.016
Received 14 May 2018; Received in revised form 22 July 2018; Accepted 24 July 2018
Available online 25 July 2018

members and veterans have achieved lesser reductions in PTSD symptoms. These results suggest that combat-related PTSD is unique. Innovative approaches are needed to augment established evidence-based treatments with targeted interventions that address the distinctive elements of combat-related traumas. This paper describes the design, methodology, and protocol of a randomized clinical trial to compare two intensive prolonged exposure therapy treatments for combat-related PTSD in active duty military service members and veterans and that can be administered in an acceptable, efficient manner in this population. Both interventions include intensive daily treatment over a 3-week period and a number of treatment enhancements hypothesized to result in greater reductions in combat-related PTSD symptoms. The study is designed to advance the delivery of care for combat-related PTSD by developing and evaluating the most potent treatments possible to reduce PTSD symptomatology and improve psychological, social, and occupational functioning.

1. Introduction

Since September 11, 2001, almost 3 million U.S. military personnel have deployed to Afghanistan, Iraq, and nearby locations. It is estimated that between 5 and 23% of these service members and veterans are at risk for the development of combat-related posttraumatic stress disorder (PTSD; [28, 35, 56]). Randomized clinical trials (RCTs) evaluating trauma-focused therapies for PTSD in civilians have demonstrated that the majority of patients achieve significant reductions in PTSD symptoms and are below diagnostic threshold for PTSD at the end of treatment [6, 34, 50, 51]. For example, Resick et al. [52] treated female civilian rape victims with PTSD using cognitive processing therapy (CPT) or prolonged exposure (PE) therapy and found that 80% of patients receiving either treatment had significant reductions in PTSD symptoms and no longer met diagnostic criteria for PTSD at the end of treatment, and their improvement was maintained for 5–10 years [55].

The treatment of combat-related PTSD in military service members and veterans, however, has proven to be more difficult [68]. Only about 40–50% of service members and veterans with combat-related PTSD achieve significant reductions in PTSD symptoms—typically defined as 10- to 12-point reductions in PTSD symptoms as assessed by self-report (e.g., PTSD Checklist; [76]) or a clinical diagnostic interview (e.g., PTSD Symptom Scale-Interview; [27])—and no longer meet the diagnostic criteria for PTSD after treatment [11–13, 25, 53, 54].

The lower efficacy in the treatment of combat-related PTSD may be due to the unique characteristics of military combat. Although some civilians also have extensive trauma histories, such as survivors of chronic childhood physical or sexual abuse by multiple perpetrators, there are some factors related to combat PTSD that are distinctly different. Compared to most instances of PTSD among civilians, combat-related PTSD may include exposure to a larger number of traumas, more complex traumas, and multiple different types of trauma [30, 69]. As a result, combat-related traumas and PTSD may be different from what is experienced by many civilians in which the frequency and variability of the traumatic experiences may be more limited. This suggests that evidence-based treatments such as CPT and PE, both of which were originally developed for survivors of sexual assault, may need to be enhanced in order to fully address the distinctive aspects of combat-related traumas.

This paper describes the design, methodology, and protocol of an RCT to compare two intensive outpatient treatments for combat-related PTSD in active duty military service members and veterans. Although intensive outpatient programs (IOPs) for PTSD are commonly used in clinical practice, no randomized clinical trial has evaluated the efficacy of this treatment format. Previous uncontrolled studies of IOPs for PTSD have been based primarily on group psychoeducation and supportive interventions and have reported minimal improvements [42]. In the present study, both treatment arms will include PE as the primary foundation of the cognitive-behavioral therapy treatment and will include 15 sessions of PE lasting 90 min each and delivered daily over a 3-week period. One treatment arm will also include a number of treatment enhancements hypothesized to improve treatment outcomes for combat-related PTSD. Many of these exposure therapy enhancements were informed by inhibitory learning theory [16, 17, 79]. The primary objectives of the study are to develop and evaluate the most potent treatments possible to reduce combat-related PTSD symptoms and long-term disabilities in psychological, social, and occupational functioning.

1.1. Research objectives and hypotheses

Project Remission: Maximizing Outcomes with Intensive Treatments for Combat-Related PTSD is one of 11 nationwide research projects supported by the Consortium to Alleviate PTSD (CAP). Headquartered at the University of Texas Health Science Center at San Antonio, the CAP was jointly funded in 2013 by the U.S. Department of Defense (DoD) and the U.S. Department of Veterans Affairs (VA). The CAP is part of a National Research Action Plan jointly issued by the Department of Defense, Department of Veterans Affairs, Department of Health and Human Services, Department of Education [18]. It has two primary objectives: (1) to develop and evaluate the most effective interventions for the treatment of combat-related PTSD and comorbid conditions in military service members and post-9/11 veterans, and (2) to study biomarkers in treatment studies to help identify the biological causes of PTSD and changes in biomarkers associated with treatment response. Additional details about the CAP are available at www.ConsortiumToAlleviatePTSD.org

The study is titled Project Remission because its primary goal is to develop and evaluate highly potent interventions capable of treating combat-related PTSD into remission. The primary research objective is to conduct a two-group randomized clinical trial to compare two intensive treatments for combat-related PTSD in military service members and veterans. Both treatments will include prolonged exposure (PE) therapy as a primary treatment component. One treatment will be a Massed-Prolonged Exposure (Massed-PE) treatment consisting of 15 daily, individual 90-min PE treatment sessions conducted over a 3-week period. Massed-PE will only include one individual PE session per day with homework and will have no other interventions throughout the treatment day. The other treatment will be an Intensive Outpatient Program-Prolonged Exposure (IOP-PE) treatment consisting of the same 15 daily, 90-min PE treatment sessions conducted over a 3-week period. However, the IOP-PE arm also will utilize eight enhancements informed by inhibitory learning theory and hypothesized to improve treatment outcomes by addressing the clinical issues that are germane to combat-related PTSD. These enhancements include: (1) the use of a team-based treatment approach; (2) clinic-based completion of daily homework assignments; (3) brief therapist feedback sessions after daily homework assignments; (4) enhanced social support; (5) focusing on patients' three most distressing traumas during imaginal exposure; (6) graduated imaginal exposure starting with the least distressing trauma; (7) an optional telescopic, brief, timeline review of all traumatic events that occurred during previous deployments; and (8) the completion of three posttreatment booster sessions. Additional details about each of these enhancements are provided in the Materials and Methods section of this manuscript. An additional research objective is to evaluate changes in disability and functional outcomes after Massed-PE and IOP-PE.