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Supplemental nicotine preloading for smoking cessation in posttraumatic stress disorder: Results from a randomized controlled trial

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HIGHLIGHTS

- Smokers with PTSD received an active or placebo patch prior to a quit attempt.
- Active patch preloading was expected to diminish nicotine-based rewards of smoking.
- Active patch was not associated with reduced craving or smoking prior to quit.
- Active patch was not associated with reduced symptom relief from smoking pre-quit.
- Active patch did not increase time to lapse or short- and long-term abstinence.

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ABSTRACT

Background: Individuals with posttraumatic stress disorder (PTSD) are more likely to smoke and more likely to relapse following a quit attempt than individuals without PTSD. Thus, there is a significant need to study promising interventions that might improve quit rates for smokers with PTSD. One such intervention, supplemental nicotine patch-preloading, entails the use of nicotine replacement therapy prior to quitting.

Objective

The objective of this study was to conduct a randomized controlled trial of the efficacy of supplemental nicotine patch-preloading among smokers with PTSD. We hypothesized that, relative to participants in the placebo condition, participants in the nicotine patch-preloading condition would: (1) smoke less and experience reduced craving for cigarettes during the nicotine patch-preloading phase; (2) experience less smoking-associated relief from PTSD symptoms and negative affect during the preloading phase; and (3) exhibit greater latency to lapse, and higher short- and long-term abstinence rates.

Methods: Sixty-three smokers with PTSD were randomized to either nicotine or placebo patch for three weeks prior to their quit date. Ecological momentary assessment was used to assess craving, smoking, PTSD symptoms, and negative affect during the preloading period.

Results: Nicotine patch-preloading failed to reduce smoking or craving during the preloading phase, nor was it associated with less smoking-associated relief from PTSD symptoms and negative affect. Moreover, no differences were observed between the treatment conditions for time to lapse, 6-week abstinence, or 6-month abstinence.

Conclusions: The findings from the present research suggest that supplemental nicotine patch-preloading is unlikely to substantially enhance quit rates among smokers with PTSD.

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Abbreviations: PTSD, posttraumatic stress disorder; NRT, nicotine-replacement therapy; EMA, ecological momentary assessment.; CBT, cognitive-behavioral therapy; CO, carbon monoxide; CAPS, Clinician Administered PTSD Scale; MDD, major depressive disorder; MNWS, Minnesota Nicotine Withdrawal Scale; MLM, multilevel modeling; CM, contingency management.

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1. Introduction

Posttraumatic stress disorder (PTSD) is a prevalent mental illness that is associated with a high rate of smoking (Beckham et al., 1997; Breslau, Davis, & Schultz, 2003; Cook, McFall, Calhoun, & Beckham, 2007; Feldner, Babson, & Zvolensky, 2007; Koenen et al., 2005; Lasser

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et al., 2000; Morissette, Tull, Gulliver, Kamholz, & Zimering, 2007; Rasmusson, Picciotto, & Krishnan-Sarin, 2006). For example, Breslau et al. (2003) found that the odds of smoking among persons with PTSD were approximately 4 times higher than persons without PTSD. Evidence from laboratory-based and ambulatory monitoring indicates that, among patients with PTSD, trauma-related stimuli, negative affect, and PTSD symptoms are associated with urges to smoke and are significant antecedents of smoking (Beckham et al., 2005; Beckham et al., 2007). Moreover, emotional reactivity to trauma-related stimuli is associated with early relapse in smokers with PTSD (Calhoun, Dennis, & Beckham, 2007). Thus, some have suggested that smoking serves as a means for managing PTSD symptoms.

Nicotine-replacement therapy (NRT) has long been used to relieve cravings during quit attempts (Fiore et al., 2008). Some have reasoned that initiating NRT prior to the quit date (*i.e.*, supplemental nicotine patch-preloading) may increase the efficacy of NRT by diminishing the reinforcing effects of inhaled nicotine, thereby making it easier to quit smoking. Rose, Behm, Westman, and Kukovich (2006) found that prior to a quit attempt smokers rated cigarettes as less rewarding when smoking while wearing nicotine patches, and that they were twice as likely to demonstrate continuous abstinence at 4 weeks post-quit than smokers who were administered a placebo patch. Other trials testing this strategy have yielded somewhat mixed results, with some (Rose, Herskovic, Behm, & Westman, 2009; Schuurmans, Diacon, van Biljon, & Bolliger, 2004), but not all (Bullen et al., 2010), reporting significantly improved long-term (*i.e.*, 6 months or more) smoking abstinence. More recently, Stead et al. (2012) conducted a review of this literature and concluded that supplemental nicotine patch-preloading resulted in a moderate increase in abstinence rates. Previous studies have excluded smokers with psychiatric conditions. To date, no study has examined the effects of supplemental nicotine patch-preloading on smoking abstinence among smokers with PTSD.

1.1. Objective and hypotheses

The objective of the present study was to conduct the first randomized controlled trial of the efficacy of supplemental nicotine patch-preloading among smokers with PTSD. Based on prior research in this area, we hypothesized that smokers with PTSD who were assigned to the nicotine patch condition would experience reduced craving for cigarettes and decreased smoking during the supplemental nicotine patch-preloading phase of the study relative to smokers who were given a placebo patch during the preloading phase of the study. We further hypothesized that smokers with PTSD assigned to the nicotine patch condition would experience significantly less smoking-associated relief from PTSD symptoms and negative affect during the patch-preloading phase of the study due to their increased levels of baseline nicotine. Finally, we hypothesized that smokers assigned to the nicotine patch-preloading condition would exhibit greater latency to lapse as well as higher six-week and six-month abstinence rates during the post-quit phase of the study relative to participants in the placebo patch condition.

2. Method

2.1. Participants

Participants were 63 individuals with PTSD. Eligibility criteria included smoking at least 10 cigarettes daily for the past year, willingness to make an attempt to quit smoking within the next 30 days, age 18–70 years, and fluency in English. Potential participants were excluded if they used non-cigarette forms of nicotine, were pregnant, had major unstable medical problems or unstable medication regimens, major respiratory disorders, used bupropion or benzodiazepines, or met criteria for current manic syndrome, current psychotic disorder, or current substance abuse/dependence including substance use in the three months immediately preceding screening.

2.2. Procedures

Participants were recruited from outpatient clinic referrals and by Institutional Review Board-approved flyers and letters advertising a study on PTSD and smoking cessation posted in local hospitals. Participants were compensated up to $650 for complete participation, including incentive payments for adhering to the ecological momentary assessment (EMA) protocol. Participants completed a screening session and one week of baseline EMA monitoring to measure *ad lib* smoking behavior. After the "*ad lib* smoking period", all participants completed a two-week "pre-quit period" during which they received either active nicotine patches or placebo patches and brief cognitive-behavioral therapy (CBT). A two-week pre-loading period is typical for prior patch pre-loading trials (Bullen et al., 2010; Rose et al., 2006; Rose et al., 1994; Rose et al., 2009; Schuurmans et al., 2004). EMA monitoring continued to track symptoms and smoking behavior for six weeks after each participant's quit date or until the participant relapsed to smoking (*i.e.*, "post-quit period"). Lapse dates and times were recorded *via* EMA and at weekly study visits. Study visits were scheduled at weeks 1–6 post-quit, during which 7-day abstinence was self-reported and verified by exhaled carbon-monoxide (CO). Participants whose CO levels exceeded 10 ppm were considered non-abstinent (Croghan, 2011). Thirty-day smoking abstinence was assessed by self-report at the six-month follow-up assessment, with positive reports of abstinence to be confirmed by saliva cotinine levels $\leq$10 ng/ml, as suggested by Benowitz (1983).

2.3. PTSD assessment

At the screening session, each participant provided sociodemographic information, smoking history, and completed the Commitment to Quitting Smoking Scale (Kahler et al., 2007), Relapse Situation Efficacy Questionnaire (Gwaltney, 2001), Fagerström Test of Nicotine Dependence (Heatherton, Kozlowski, Frecker, & Fagerström, 1991). PTSD was assessed with the Clinician Administered PTSD Scale (CAPS; Blake et al., 1995), using established guidelines (Weathers & Keane, 1999). The presence of current major depressive disorder (MDD) was assessed with the Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Patient Edition (First, Spitzer, Gibbon, & Williams, 1996). Study interviewers completed an extensive training program, demonstrating strong inter-rater reliability at its completion on seven video-recorded interviews (Fleiss' kappa = 0.96).

2.4. Randomization to nicotine preloading treatment groups

Randomization to active nicotine patch or placebo patch was stratified by gender and presence of current MDD. Participants were randomized to receive either 21 mg/24 h patch or placebo for 2 weeks prior to a target quit date in a double blind fashion. Patch allocation was concealed by maintaining a list through the pharmacy that was unavailable to study investigators and coordinators.

2.5. Behavioral counseling and post-quit NRT

During the pre-quit period, all participants received two individual sessions of cognitive-behavioral smoking-cessation counseling. CBT counseling sessions lasted 50 min each and included psychoeducation about the physiological effects of smoking, behavioral strategies for coping with withdrawal symptoms, relaxation training, identification of social support, plans for reinforcing abstinence and relapse prevention. Beginning at the quit date, all participants received six weeks of active nicotine replacement therapy (starting with 21 mg/24 h nicotine