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Predictors of induction onto extended-release naltrexone among unemployed heroin-dependent adults

Brantley P. Jarvis, August F. Holtyn, Meredith S. Berry, Shrinidhi Subramaniam, Annie Umbricht, Michael Fingerhood, George E. Bigelow, Kenneth Silverman *

Johns Hopkins University School of Medicine, United States

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ABSTRACT

Background and aim: Extended-release naltrexone (XR-NTX) blocks the effects of opioids for 4 weeks; however, starting treatment can be challenging because it requires 7 to 10 days of abstinence from all opioids. In the present study we identified patient and treatment characteristics that were associated with successful induction onto XR-NTX.

Methods: 144 unemployed heroin-dependent adults who had recently undergone opioid detoxification completed self-report measures and behavioral tasks before starting an outpatient XR-NTX induction procedure. Employment-based reinforcement was used to promote opioid abstinence and adherence to oral naltrexone during the induction. Participants were invited to attend a therapeutic workplace where they earned wages for completing jobs skills training. Participants who had used opioids recently were initially invited to attend the workplace for a 7-day washout period. Then those participants were required to provide opioid-negative urine samples and then take scheduled doses of oral naltrexone to work and earn wages. Participants who had not recently used opioids could begin oral naltrexone immediately. After stabilization on oral naltrexone, participants were eligible to receive XR-NTX and were randomized into one of four treatment groups, two of which were offered XR-NTX. Binary and multiple logistic regressions were used to identify characteristics at intake that were associated with successfully completing the XR-NTX induction.

Results: 58.3% of participants completed the XR-NTX induction. Those who could begin oral naltrexone immediately were more likely to complete the induction than those who could not (79.5% vs. 25.0%). Of 15 characteristics, 2 were independently associated with XR-NTX induction success: legal status and recent opioid detoxification type. Participants who were not on parole or probation (vs. on parole or probation) were more likely to complete the induction (OR [95% CI] = 2.5 [1.1–5.7], $p = 0.034$), as were those who had come from a longer-term detoxification program (≥21 days) (vs. a shorter-term [<21 days]) (OR [95% CI] = 7.0 [3.0–16.6], $p < 0.001$).

Conclusions: Our analyses suggest that individuals recently leaving longer-term opioid detoxification programs are more likely to complete XR-NTX induction. Individuals on parole or probation are less likely to complete XR-NTX induction and may need additional supports or modifications to induction procedures to be successful.

1. Introduction

Rising rates of overdose and opioid use disorder caused by nonmedical prescription opioid use and heroin are significant public health issues in the United States (Han et al., 2015; Jones et al., 2015). Although underutilized, medication-assisted treatment including methadone (agonist), buprenorphine (partial agonist), and naltrexone (antagonist) is critical to and effective in managing the chronic relapsing nature of opioid use disorder (Connery, 2015; Substance Abuse and Mental Health Service Administration [SAMHSA], 2014). Methadone and buprenorphine are the most commonly used medications to treatment opioid use disorder; however, naltrexone is preferred by some patients (Uebelacker et al., 2016) and may be more suitable for certain situations because it blocks the subjective and physiological effects of opioids (Bigelow et al., 2012), cannot produce lethal overdose or be abused, does not have special prescribing regulations (SAMHSA, 2015), and can be delivered as a monthly injection (extended-release naltrexone; XR-NTX) to address poor compliance associated with its oral formulation (Brooks et al., 2010).

Despite these advantages, initiating XR-NTX treatment can be challenging. Unlike methadone and buprenorphine, XR-NTX requires 7 to 10 days of abstinence from all opioids prior to beginning the medication to prevent potentially serious precipitated withdrawal (Alkermes®,

* Corresponding author at: 5200 Eastern Avenue, Center for Learning and Health, Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, MD 21224, United States.
E-mail address: ksilverm@jhmi.edu (K. Silverman).

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2015). Most patients relapse quickly following inpatient (Smyth et al., 2010) and during outpatient buprenorphine-assisted detoxification (Dunn et al., 2011), and would not be eligible for XR-NTX. The subset of patients who are able to abstain throughout a recent buprenorphine-assisted detoxification must continue to remain opioid-free following buprenorphine taper and termination. This post-detoxification period is particularly challenging and has been associated with heightened withdrawal and relapse (Dunn et al., 2011; Horspool et al., 2008; Sullivan et al., 2017).

As an alternative to requiring 7 to 10 days of opioid abstinence, efforts to increase the number of patients who could receive XR-NTX thus far have focused on developing rapid opioid detoxification procedures and evaluating investigational non-opioid medications to ease withdrawal (memantine and dronabinol, Bisaga et al., 2014, 2015). These procedures last 8 days; can occur in both inpatient and outpatient settings; and include brief buprenorphine stabilization, a washout period, and gradually increasing doses of oral naltrexone with XR-NTX delivery on the final day. Precipitated withdrawal symptoms are treated with non-opioid medications such as clonidine, clonazepam, zolpidem, trazodone, and other adjuvant medications. A similar outpatient rapid detoxification procedure that combines increasing very low dose oral naltrexone with decreasing low doses of buprenorphine has also been evaluated (Mannelli et al., 2014). The investigational medications memantine and dronabinol have had no effect on XR-NTX induction outcomes. The rapid detoxification procedures in the above studies produced XR-NTX induction rates between 56% and 70%, and a recent outpatient randomized clinical trial showed that rapid outpatient naltrexone-assisted detoxification was superior to buprenorphine-only detoxification in promoting transition to XR-NTX (Sullivan et al., 2017).

In addition to developing optimal opioid detoxification protocols to promote XR-NTX induction, researchers and clinicians could further benefit from identifying treatment and patient characteristics that are associated with successful XR-NTX induction. Such information could inform clinical decision making, incorporate more personalized care, and potentially improve treatment outcomes. Few studies have examined patient characteristics predicting successful naltrexone induction. Those that have showed that older patients who used less opioids (Mogali et al., 2014), who were less prone to risk-taking (Aklin et al., 2012), and who used prescription opioids (Sullivan et al., 2017) were more likely to complete naltrexone induction than younger patients who used more opioids, were more prone to risk-taking, and who used heroin. The purpose of the current study was to extend this line of research by exploring predictors of XR-NTX induction among unemployed heroin-dependent adults enrolled in a randomized clinical trial to treat heroin use.

2. Materials and methods

2.1. Main trial overview

Data were collected as part of an ongoing randomized clinical trial to evaluate the separate and combined effects of employment-based opiate abstinence reinforcement and XR-NTX for heroin use. Participants who completed the induction (described below) were invited to a 24-week outpatient treatment in a therapeutic workplace (for a description of the therapeutic workplace, see Silverman et al., 2016) and were randomized to one of four treatment conditions, two of which involved treatment with XR-NTX. All data were collected between November 2012 and June 2016.

2.2. Participants

Participants were recruited from detoxification programs in Baltimore, MD, through street outreach, from programs that provide services to heroin-dependent adults, and by word of mouth. Inclusion criteria for the main trial were that participants: (1) met DSM-IV criteria for opioid dependence, (2) reported using heroin at least 21 of the last 30 days while living in the community, (3) reported and show visible signs (track marks) of injection drug use, (4) were unemployed, (5) were between 18 and 65 years old, (6) were medically approved for naltrexone treatment, and (7) lived in or near the study area. Exclusion criteria were that participants: (1) had current DSM-IV major Axis I disorders, (2) had current suicidal or homicidal ideation, (3) expressed interest in methadone or buprenorphine maintenance treatment, (4) used opioids for prescribed medical purposes, (5) earned over $200 in taxable income in the past 30 days while living in the community, (6) had physical limitations that prevented them from using a keyboard, (7) were pregnant or breastfeeding, (8) had serum aminotransferase levels over three times normal, (9) had known intolerance to naltrexone or XR-NTX components, and (10) were enrolled in another clinical study.

The requirement that participants be injection drug users was removed on January 2015 to broaden the target population and increase enrollment. For the present analyses, only eligible participants who formally enrolled in the main trial were included (i.e., those who signed a consent but never returned were excluded).

2.3. Intake assessments

At an intake session, participants completed a battery of self-report measures and interviews, behavioral tasks, and provided a urine sample that was tested for opiates, methadone, buprenorphine, oxycodone, cocaine, benzodiazepines, and THC.

2.3.1. Self-report measures and interviews

Self-report measures and interviews included the following: (1) Addiction Severity Index-Lite (ASI; McLellan et al., 1985), a semi-structured interview that assesses functioning in multiple dimensions (i.e., substance use, medical, legal, education, employment, and family histories); (2) Composite International Diagnostic Interview (CIDI; heroin and cocaine sections only; Compton et al., 1996), a valid DSM-IV diagnostic tool for psychiatric disorders; (3) Beck Depression Inventory-II (Beck et al., 1996) a 21-item measure of depression severity; and (4) Prior treatment form, a questionnaire to gather information on participant's most recent opioid detoxification. Participants were categorized as coming from shorter-term (<21 days) or longer-term (≥21 days) detoxification programs. Three participants had recently been released from incarceration (≥21 days) and were categorized as longer-term. All longer-term detoxifications were inpatient programs, whereas short-term detoxifications were a mix of outpatient and inpatient programs. Specific details on detoxification protocols and medications were not collected.

2.3.2. Behavioral tasks

Behavioral tasks included the Balloon Analogue Risk Task (BART; Lejuez et al., 2002), a delay discounting task, and the Wisconsin Card Sorting Task (WCST; Heaton et al., 1993). The BART is a computer-based task that measures risk-taking propensity. The task displays a simulated balloon, a balloon pump button, an earnings collection button, a current earnings display, and a total earnings display. Participants were instructed to pump the simulated balloon to earn as much money as possible but to keep in mind that the balloon could pop at any time. Each click on the pump button increases the size of the simulated balloon and adds money ($0.05) to a current earnings display. Balloons that are pumped beyond their individual explosion points pop, and money accrued in the current earnings display is lost. Explosion points ranged from 1 to 128 pumps and were randomly determined for each balloon. At any time during the task, participants could collect their current earnings by pressing the earnings collection button. After a balloon was popped or earnings were collected, a new trial began with a new balloon, ending on the 20th trial. The primary measure of risk-taking

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