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Patient characteristics associated with buprenorphine/naloxone treatment outcome for prescription opioid dependence: Results from a multisite study☆

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ABSTRACT

Background: Prescription opioid dependence is a growing problem, but little research exists on its treatment, including patient characteristics that predict treatment outcome.
Methods: A secondary analysis of data from a large multisite, randomized clinical trial, the National Drug Abuse Treatment Clinical Trials Network Prescription Opioid Addiction Treatment Study (POATS) was undertaken to examine baseline patient characteristics ($N = 360$) associated with success during 12-week buprenorphine/naloxone treatment for prescription opioid dependence. Baseline predictor variables included self-reported demographic and opioid use history information, diagnoses assessed via the Composite International Diagnostic Interview, and historical opioid use and related information from the Pain And Opiate Analgesic Use History.
Results: In bivariate analyses, pre-treatment characteristics associated with successful opioid use outcome included older age, past-year or lifetime diagnosis of major depressive disorder, initially obtaining opioids with a medical prescription to relieve pain, having only used opioids by swallowing or sublingual administration, never having used heroin, using an opioid other than extended-release oxycodone most frequently, and no prior opioid dependence treatment. In multivariate analysis, age, lifetime major depressive disorder, having only used opioids by swallowing or sublingual administration, and receiving no prior opioid dependence treatment remained as significant predictors of successful outcome.
Conclusions: This is the first study to examine characteristics associated with treatment outcome in patients dependent exclusively on prescription opioids. Characteristics associated with successful outcome after 12 weeks of buprenorphine/naloxone treatment include some that have previously been found to predict heroin-dependent patients' response to methadone treatment and some specific to prescription opioid-dependent patients receiving buprenorphine/naloxone.

1. Introduction

Misuse of prescription opioids is a growing problem in the United States, with nonmedical prescription opioid use second only to marijuana in prevalence of use among illicit drugs. In 2010, 5.1 million Americans aged 12 or older (2.0%) reported past-month nonmedical prescription opioid use. After marijuana, prescription

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opioids had the second highest levels of past-year dependence or abuse, with 1.9 million people meeting criteria for these disorders (Substance Abuse and Mental Health Services Administration, 2011). Prescription opioid abuse is well-represented in treatment-seeking populations, with 9.8% of substance abuse treatment admissions reporting prescription opioid abuse, representing more than a fourfold increase between 1998 and 2008. More than a quarter of patients entering medication-assisted opioid therapy in 2008 were primarily using prescription opioids (Substance Abuse and Mental Health Services Administration, 2010).

Despite increasing rates of prescription opioid abuse and dependence (Arfken et al., 2010), most research on opioid dependence treatment has focused primarily on heroin-dependent patients receiving methadone maintenance treatment. Research has suggested, though, that compared to patients dependent on heroin, prescription opioid-dependent patients have characteristics associated with a more favorable response to treatment; these include shorter opioid use histories, less prior treatment, higher income, greater social stability, and less opioid use per day (Moore et al., 2007; Sigmon, 2006). Indeed, Moore et al. (2007) found that patients dependent on prescription opioids fared better than heroin-dependent patients with office-based buprenorphine/naloxone pharmacotherapy. Given this potential differential response to treatment between prescription opioid and heroin users, it is important to identify factors associated with better treatment outcome for patients dependent on prescription opioids.

Studies of predictors of treatment outcome in opioid dependence have employed various measures of outcome, including treatment retention (Mancino et al., 2010), rates of positive urine drug screens (Alterman et al., 1998), continuous opioid abstinence (Darke et al., 2005), and Addiction Severity Index composite scores (Cacciola et al., 2001). Studies of patient characteristics associated with treatment outcome have often focused on sociodemographic factors, drug use history, psychiatric history, and other areas of functioning. Although not all studies agree, characteristics most consistently associated with poorer outcome among heroin-dependent patients in methadone maintenance treatment include younger age (Mancino et al., 2010; Strain et al., 1998), Black or non-White race (Iguchi and Stitzer, 1991; Marsch et al., 2005), male gender (Iguchi and Stitzer, 1991; Schottenfeld et al., 1998), being unmarried/not living with a stable partner (McLellan, 1983; Torrens et al., 1996), cocaine use (Joe et al., 1999; Williamson et al., 2007), problematic and/or frequent alcohol use (Flynn et al., 2003; Stenbacka et al., 2007), more frequent baseline opioid use (Darke et al., 2005; Strain et al., 1998), more frequent injection use (Darke et al., 2005; Simpson et al., 1997), more previous treatment (Hser et al., 1999; Teesson et al., 2008), comorbid substance use disorders (Marsch et al., 2005; Peles et al., 2010), more severe psychiatric problems (Gelkopf et al., 2006; Joe et al., 1994), personality disorders (Alterman et al., 1996; Cacciola et al., 2001), poorer psychosocial functioning (Gerra et al., 2004; Hser et al., 1999), and more severe criminal and legal involvement (Favrat et al., 2002; Flynn et al., 2003). There have been conflicting results about depression as a predictor of treatment outcome; a diagnosis of depression has alternately been associated with both better (Rao et al., 2004) and worse (Teesson et al., 2008) outcome of methadone maintenance treatment.

Despite its demonstrated efficacy (Johnson et al., 2000) and increasingly wide use (Arfken et al., 2010) in opioid dependence treatment, the literature on characteristics associated with outcome of buprenorphine (as opposed to methadone) treatment is more limited, as buprenorphine was not available to treat opioid dependence until 1996 in Europe and 2003 in the United States. Studies examining characteristics associated with buprenorphine treatment outcome have primarily concurred with those examining methadone maintenance treatment. Younger age (Marsch et al., 2005; Soyka et al., 2008), male gender (Marsch et al., 2005; Schottenfeld et al., 1998), cocaine use (Sullivan et al., 2010) or dependence (Marsch et al., 2005), longer histories of opioid use (Soyka et al., 2008), more severe psychiatric problems (Pani et al., 2000; Petry and Bickel, 1999), poorer psychosocial functioning (Pani et al., 2000; Resnick et al., 1991), and more severe legal problems (Petry and Bickel, 2000) have been associated with poorer buprenorphine treatment outcome. Depression has been found to be associated with better outcome of buprenorphine treatment (Gerra et al., 2004; Marsch et al., 2005), corroborating Rao and colleagues' (2004) results in their study of methadone treatment.

Given the growing problem of prescription opioid dependence and the potential differences between prescription opioid and heroin users in response to treatment, there is a need to determine characteristics of patients dependent on prescription opioids that may predict their response to buprenorphine treatment. Patient characteristics associated with treatment outcome in studies of heroin users receiving methadone or buprenorphine treatment may not be the same in prescription opioid-dependent patients, who differ in their sociodemographic characteristics as well as their drug use patterns (e.g., obtaining opioid prescriptions from physicians for pain, less injection use). The current study thus examined data from the National Drug Abuse Treatment Clinical Trials Network Prescription Opioid Addiction Treatment Study (POATS; Weiss et al., 2011), a large multisite randomized clinical trial, to identify patient characteristics associated with success during a 12-week buprenorphine treatment period.

2. Methods

2.1. Main study objectives and design

The primary objectives of POATS were to examine the added benefit of counseling to buprenorphine/naloxone treatment of prescription opioid dependence and to help identify the optimal length of pharmacological treatment for this population (detoxification versus maintenance treatment). The main study used a randomized, two-phase adaptive treatment research design (Fig. 1; Murphy et al., 2007) at ten sites across the United States. Following brief buprenorphine/naloxone treatment, consisting of induction, 2 weeks of stabilization, and a 2-week taper (Phase 1), participants who returned to opioid use were invited to enter Phase 2, consisting of 12 weeks of buprenorphine/naloxone stabilization, followed by a 4-week taper and 8-week post-treatment follow-up (Weiss et al., 2010b). In both phases, participants were randomized to either (1) Standard Medical Management alone (SMM; Fiellin et al., 1999), or (2) SMM plus individual Opioid Dependence Counseling (SMM + ODC; Pantalon et al., 1999). Participants were stratified in Phase 1 by (1) presence of current chronic pain and (2) a lifetime history of heroin use. In Phase 2, participants were stratified by the condition to which they were assigned in Phase 1.

2.2. Study population

Participants in Phase 1 met DSM-IV (American Psychiatric Association, 2000) criteria for current opioid dependence and were at least 18 years old. Key exclusion criteria included any of the following: heroin use on ≥4 days in the past month; a lifetime diagnosis of opioid dependence due to heroin alone; a history of ever injecting heroin; or concurrent formal ongoing substance abuse treatment (see Weiss et al. (2010b) for details). Patients who were currently prescribed opioids for pain needed permission from their prescribing physician to enter the study. Of the 653 participants enrolled in Phase 1, 360 went on to Phase 2. The current study population includes only the 360 participants who were unsuccessful in Phase 1 and subsequently enrolled in Phase 2.

2.3. Treatments

Participants in each phase were inducted onto sublingual buprenorphine/naloxone, receiving 4–12 mg on the day of induction, and once-daily doses ranging from 8 to 32 mg per day for the subsequent duration of stabilization treatment (2 weeks in Phase 1, 12 weeks in Phase 2). At each SMM visit, the study physician could adjust the dose by increments up to 8 mg/wk. All participants received manual-based SMM, which has previously demonstrated efficacy when used in a primary care setting (O'Connor et al., 1998), in a 30–60 min initial session and subsequent 15–20 min sessions. In addition to SMM, half of the participants were randomly assigned to receive manual-based ODC (Pantalon et al., 1999), administered in 45–60 min sessions by trained substance abuse or mental health professionals. In Phase 1, ODC occurred twice per week. In Phase 2, ODC was