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Buprenorphine pharmacotherapy and behavioral treatment: Comparison of outcomes among prescription opioid users, heroin users and combination users

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ABSTRACT

Most research examining buprenorphine has been conducted with heroin users. Few studies have examined buprenorphine pharmacotherapy for prescription opioid users. Data were from a randomized controlled trial of behavioral treatment provided for 16 weeks on a platform of buprenorphine pharmacotherapy and medication management. We compared heroin (H, $n = 54$), prescription opioid (PO, $n = 54$) and combination heroin + prescription opioid (POH, $n = 71$) users to test the hypothesis that PO users will have better treatment outcomes compared with heroin users. The PO group provided more opioid-negative urine drug screens over the combined treatment period (PO:70%, POH:40%, H:38%, $p < 0.001$) and at the end of the combined treatment period (PO:65%, POH:31%, H:33%, $p < 0.001$). Retention was lowest in the H group (PO:80%, POH:65%, H:57%, $p = 0.039$). There was no significant difference in buprenorphine dose between the groups. PO users appear to have better outcomes in buprenorphine pharmacotherapy compared to those reporting any heroin use, confirming that buprenorphine pharmacotherapy is effective in PO users.

1. Introduction

An increasing population of prescription opioid (PO) users in the United States is well documented (Compton & Volkow, 2006; Maxwell, 2011). With the increased use of prescription opioids, there has been a growing demand for treatment for PO dependence (Fischer, Nakamura, Rush, Rehm, & Urbanoski, 2010), and the high mortality associated with PO dependence (Paulozzi, 2012; Warner, Chen, & Makuc, 2009) suggests an urgent need for empirical research to identify effective treatments.

Buprenorphine pharmacotherapy is well-established for the treatment of illicit opioid dependence (Amass, Kamien, & Mikulich, 2000; Ling & Wesson, 2003; Ling, Wesson, Charuvastra, & Klett, 1996; Mattick, Kimber, Breen, & Davoli, 2008). Buprenorphine has an advantageous safety profile including a low risk of respiratory depression (Walsh, Preston, Stitzer, Cone, & Bigelow, 1994), and its availability in primary care or other office based settings makes it an ideal candidate for treating PO dependence. Depending on the treatment setting, buprenorphine also allows medication by prescription to be taken at home, thereby avoiding daily attendance at opioid treatment programs, which may be a potential barrier for treatment.

Several studies have assessed the use of buprenorphine for PO dependence and found that PO users have similar induction experiences compared to heroin users, and require similar doses of buprenorphine (Nielsen, Hillhouse, Mooney, Fahey, & Ling, 2012). More PO users were able to successfully complete a buprenorphine taper compared to heroin users (Nielsen, Hillhouse, Thomas, Hasson, & Ling, 2013), although a large study examining short and intermediate buprenorphine pharmacotherapy for PO users found that 93% of participants relapsed to opioid use after a 2-week stabilization period and 2-week taper, and after receiving a 12-week stabilization and 4-week taper, 91% had relapsed when followed up 8 weeks post taper (Weiss et al., 2011). There is a lack of research to inform longer-term outcomes in buprenorphine pharmacotherapy for PO users.

One retrospective case series compared treatment outcomes for heroin users and PO users in office-based buprenorphine pharmacotherapy (Moore et al., 2007), and found that PO users had better treatment outcomes with regard to opioid-negative urine tests and retention. Heroin use in a sample of PO users was found to be a negative predictor of outcomes (Weiss et al., 2011). To the authors' knowledge, however, no study has compared outcomes for PO and heroin users using clinical outcome data from a clinical treatment study.

Favorable treatment outcomes for PO users may be related to differences observed between PO users and heroin users. A

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retrospective review of PO users entering methadone treatment found that PO users were more likely to have ongoing pain and mental health problems compared to heroin users, although no differences were detected on measures of social stability (Brands, Blake, Sproule, Gourlay, & Busto, 2004). Moore et al. (2007) found that PO users had shorter opioid use and treatment histories, with heroin users having used opioids for around 5 years longer, and most (59%) reporting more than one previous treatment attempt, compared to 29% of PO users. PO users were more likely to be white, have higher income, and be hepatitis C antibody negative. Fischer, Patra, Cruz, Gittins, and Rehm (2008) also found that opioid-dependent patients using only PO were more likely to be white and have legal income, although some patterns of polysubstance use were identified in the PO use groups. These studies demonstrate important differences in opioid use history and resources (social and financial) that exist between PO and heroin users. These studies find that PO users appear to do well in treatment with characteristics such as employment that bode well for successful treatment outcomes (Brewer, Catalano, Haggerty, Gainey, & Fleming, 1998; Heinrich & Fournier, 2005).

The current secondary analysis addresses treatment outcomes compared across three opioid use groups using data from a recently completed clinical trial. We hypothesize that PO users who do not use heroin will have better treatment outcomes compared with those who use a combination of PO and heroin, or who use heroin alone.

2. Methods

2.1. Design

This secondary analysis forms part of a planned series of analysis to examine buprenorphine pharmacotherapy outcomes in previously conducted clinical trials that included heroin and PO users. The parent study was a randomized controlled trial to test the comparative efficacy of four behavioral treatment conditions provided for 16 weeks on a platform of pharmacotherapy and medication management for the treatment of opioid dependence (Ling, Hillhouse, Ang, Jenkins, & Fahey, 2013) (Clinical Trials Registration: NCT00591617). Study participants received buprenorphine (as Suboxone®) and medication management (MM), an approximation of the care provided by physicians when prescribing buprenorphine in private practice, and were randomized to one of four behavioral conditions: cognitive behavioral therapy (CBT), contingency management (CM), both CBT + CM, and MM alone. Descriptions of the main study and study findings are published elsewhere (Ling et al., 2013).

Potential participants were consented and screened for eligibility, inducted and stabilized on buprenorphine for 2 weeks, and were then assigned to a behavioral condition for a 16-week combined treatment phase of pharmacotherapy and behavioral treatment. A subsequent second 16-week medication-only phase followed. Follow-up assessments were administered at weeks 40 and 52.

2.2. Participants

Recruitment methods included advertising, word-of-mouth, study announcement flyers posted in treatment programs and community locations, and referrals such as from local narcotic treatment and outreach programs, alcohol and drug abuse clinics, primary care providers, and mental health centers.

Eligibility criteria included being at least 15 years of age, meeting the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition—Text Revision* (*DSM-IV-TR*) criteria for opioid dependence (American Psychiatric Association, 2000), being of general good medical and psychiatric health, with no sensitivity to buprenorphine or naloxone, and no pattern of alcohol, benzodiazepine or other drug use that would require immediate medical attention or be unsafe in the context of the study. Female participants could not be pregnant or nursing, and must have agreed to use an acceptable method of birth control. A total of $410 compensation was provided for completing all assessments (see Ling et al., 2013 for further details).

For this analysis, participants were classified as prescription opioid only (PO), prescription opioid and heroin (POH) and heroin only (H) based on self-reported opioid use in the 30 days prior to screening.

2.3. Procedures

2.3.1. Screening

Appointments were made with interested individuals who met preliminary screening criteria. After voluntarily signing informed consent, participants were assessed to determine eligibility and to provide baseline information. All procedures followed were in accord with the Helsinki Declaration of 1975.

Eligible participants met with a study physician to review a Suboxone Treatment Information sheet outlining proper use of medication for take-home dosing; a Handbook for Recovery from Opiate Dependence, developed by the PI; a Suboxone Treatment Information booklet provided by the manufacturer of the study medication; and a wallet card that identified the participant as being in a clinical research study.

2.3.2. Medication induction and randomization

Suboxone, a combination of buprenorphine and naloxone in a 4:1 ratio taken sublingually, was used in this trial. Participants were inducted onto buprenorphine starting at 4 mg (expressed as amount of buprenorphine), and stabilized over 2 weeks. On day 1 a 4 mg dose was dispensed in the clinic and monitored by medical personnel to assess any adverse effects. An additional 2–4 mg dose could be provided at the study physician's discretion. The total dose for day 1 was 8–16 mg. Day 2 induction doses ranged between 8 and 16 mg, and day 3 doses ranged between 12 and 24 mg. Induction procedures are described in detail elsewhere (Nielsen et al., 2012).

After induction, the daily dosage could be adjusted to range from 2 to 24 mg for the balance of the 2-week induction/stabilization phase. At the end of this phase, participants were randomized to behavioral condition. Participants were not stratified by opioid category (PO; POH; H), however there was no significant difference in the percentages of the three opioid group types randomized to each condition.

2.3.3. Pharmacotherapy and behavioral therapy phase

During the 16-week combined-treatment phase, participants were scheduled to attend clinic twice weekly for collection of data and urine specimens and to receive study medication. Participants also met weekly with the study physician for medication management, and attended their assigned behavioral therapy (CBT, CM). All participants received weekly medication management and, during these sessions, dose adjustments and limited discussion of progress, symptoms, and medication issues as normally provided to patients in private office-based practice settings were provided by study physicians. Weekly CBT sessions focused on relapse prevention skills, and CM was administered twice weekly to provide incentives for opioid-negative urine drug screens (UDS).

2.3.4. Medication only phase, taper and follow up

Participants attended the clinic weekly after the combined treatment phase through week 40 for data collection, medication management visits, and UDS. Between weeks 34 and 40 participants were tapered off buprenorphine. Study physicians were encouraged to reduce the buprenorphine dose over 1 week per previous research showing no advantage in prolonging taper (Ling et al., 2009). However, participants could request up to 6 weeks to finish their taper. Participants could have been referred to pharmacotherapy at the study physician's discretion, rather than entering the taper phase.