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Substance Use and Response to Psychiatric Treatment in Methadone-Treated Outpatients with Comorbid Psychiatric Disorder

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ABSTRACT

The psychiatric care of opioid users receiving agonist therapies is often complicated by high rates of illicit drug use (Brooner et al., 2013). The present study evaluates if illicit drug use (i.e., opioids, cocaine, sedatives) detected at the start of psychiatric care affects treatment response. Methadone maintenance patients ($n = 125$) with at least one current psychiatric disorder completed a 3-month randomized clinical trial evaluating the efficacy of financial incentives on attendance to on-site integrated substance abuse and psychiatric services (Kidorf et al., 2013). The present study re-analyzes the data set by grouping participants into one of two conditions based on the 4-week baseline observation: (1) no illicit drug use (baseline negative; $n = 50$), or (2) any illicit drug use (baseline positive; $n = 75$). All participants received a similar schedule of psychiatric services, and had good access to prescribed psychiatric medications. The Global Severity Index (GSI) of the Hopkins Symptom Checklist-Revised was administered monthly to evaluate changes in psychiatric distress. Results showed that while both conditions evidenced similar utilization of on-site psychiatric services, baseline negative participants remained in treatment somewhat longer (80.7 vs. 74.8 days, $p = .04$) and demonstrated greater reductions in GSI scores than baseline positive participants at month 3 ($p = .004$). These results have implications for interpreting previous studies that have shown inconsistent efficacy of pharmacotherapy and other psychiatric treatments, and for providing clinical care for patients with co-occurring substance use and psychiatric disorders.

1. Introduction

Opioid-dependent individuals experience much higher rates of co-occurring psychiatric disorders than the general population (Brooner, King, Kidorf, Schmidt, & Bigelow, 1997; Kessler, Chiu, Demler, Merikangas, & Walters, 2005; Strain, 2002). Well over half have at least one co-occurring psychiatric disorder, with major depression and antisocial personality disorder (APD) generally found to be the most prevalent conditions (Brooner et al., 1997; Kidorf et al., 2004; McGovern, Xie, Segal, Siembab, & Drake, 2006). Numerous studies have shown that psychiatric comorbidity in opioid-dependent individuals is associated with considerable psychiatric distress, higher rates of lifetime and current substance use disorder, and often a poorer response to substance abuse treatment (Brooner et al., 1997; Cacciola, Alterman, Rutherford, McKay, & Mulvaney, 2001; Compton, Cottler, Jacobs, Ben-Abdallah, & Spitznagel, 2003; Darke et al., 2007; Kidorf et al., 2004).

Unfortunately, less is known about effective strategies to treat psychiatric comorbidity in people with opioid dependence. Two major categories of studies have evaluated the efficacy of psychiatric treatment in this population. Placebo-controlled medication trials, most often conducted with those experiencing major depression or elevated depression symptom severity, have produced very mixed results. For example, Nunes et al. (1998) showed that 57% of depressed methadone maintenance patients completing at least 6-weeks of an imipramine trial were rated as clinically improved (compared to only 7% of the placebo condition), though few patients demonstrated abstinence in routine urinalysis testing. Other studies show little advantage of pharmacotherapy versus placebo in reducing either psychiatric symptoms or drug use (Carpenter, Brooks, Vosburg, & Nunes, 2004; Kleber et al., 1983; Petrakis et al., 1998; see Nunes & Levin, 2004 and Pedrelli et al., 2011, for reviews). A second category of studies evaluating varying models of integrated psychiatric and substance abuse treatment have shown some promise (Brooner et al., 2013), though most studies of integrated care for combinations of opioid users and other substance users have reported little benefit compared to parallel or sequential models of care (see Donald, Dower, & Kavanaugh, 2005, for a review).

It is possible that variation in response to placebo-controlled trials and integrated care in this population may be associated with current substance use. Treatment-seeking opioid users commonly use cocaine and sedatives (Chutuape, Brooner, & Stitzer, 1997; Epstein et al., 2009; Lintzeris & Nielsen, 2010; Peirce et al., 2006). Ongoing substance use might affect adherence and/or response to psychiatric services. The correlation between adherence and psychiatric treatment response

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was illustrated nicely in a randomized trial of pharmacotherapy and cognitive–behavioral therapy for depressed injection drug users not receiving substance abuse care (Stein et al., 2004). Current substance use might also be associated with more severe psychosocial problems and impoverished environments, thereby reducing the effectiveness of both psychosocial and medication interventions for comorbid psychiatric problems (Carpenter et al., 2004).

While illicit drug use is frequently implicated as a predictor of poorer response to substance abuse treatment in this population (Kidorf, Brooner, King, & Stoller, 1998; Saxon, Wells, Fleming, Jackson, & Calsyn, 1996), it has not been examined as a predictor of response to psychiatric treatment. In addition, study of the impact of substance use on psychiatric treatment response may help explain the inconsistent findings of previous studies, and potentially help establish conditions required for optimal response to psychiatric treatment. For example, one concern related to drug use during episodes of psychiatric care is that many integrated care approaches appear to reduce the amount of time and focus on substance use to make time to address the comorbid psychiatric condition (Donald et al., 2005). Evidence that current substance use reduces response to psychiatric treatment for the comorbid disorder might caution against the development of integrated care approaches that dilute attention to the substance use problem.

We recently completed a 3-month randomized clinical trial evaluating the efficacy of financial incentives on attendance to on-site integrated psychiatric treatment for methadone maintenance patients (Kidorf et al., 2013). The present study re-analyzes this dataset by grouping participants on the absence or presence of illicit drug use in urine samples tested during the 1-month study baseline, and evaluating condition differences on psychiatric service utilization and psychiatric treatment response over the observation period. We hypothesized that participants using illicit drugs at baseline would have poorer psychiatric service utilization and response to treatment.

2. Methods

2.1. Participants

Study participants were 125 opioid-dependent outpatients enrolled in a community-based opioid-agonist clinic and recruited from 12/15/09 to 4/30/12. Patients were eligible to participate if they reported psychiatric concerns consistent with a current psychiatric disorder to their substance abuse counselor, and expressed interest in receiving psychiatric treatment offered within the program. Exclusion criteria included: (1) pregnancy, (2) experiencing an acute medical or psychiatric problem that required immediate and intense intervention, or (3) having severe cognitive impairment that interfered with understanding study procedures. The Johns Hopkins University Institutional Review Board approved the study.

Patients providing informed written consent to participate in the evaluation ($n = 158$) were informed of the requirements, risks, and benefits of study participation. Participants were excluded from randomization if they: (1) failed to meet criterion for a current psychiatric disorder on the SCID interview and subsequent clinical reappraisal done by one of the co-investigators ($n = 4$); (2) left the treatment program prior to randomization ($n = 13$); (3) failed to complete study assessments ($n = 3$); (4) exhibited poor cognitive functioning or acute medical concerns ($n = 5$); (5) reported receiving psychiatric care elsewhere ($n = 1$). An additional seven participants withdrew from the study for unspecified reasons, leaving a randomized sample pool of 125 participants.

Table 1 (column 1) reports baseline demographic and psychiatric characteristics, methadone dose, and urinalysis results for the sample. Participants were maintained on average of 84.6 mg ($SD = 23.3$) of methadone. Major depression and post-traumatic stress disorder (PTSD) were the most prevalent Axis I psychiatric disorders; 42% were diagnosed with antisocial personality disorder (APD). Only one participant was diagnosed with a substance-induced psychiatric disorder (i.e., psychiatric symptoms developed within a month of a clinically notable change in the frequency or amount of substance use which appeared sustained by the change).

2.2. Assessments

Participants completed the Structured Clinical Interview for the *DSM-IV-R* (SCID-I and SCID-II; First, Spitzer, Gibbon, & Williams, 1995) during the second week of baseline. The SCID-I is a structured interview that uses a decision-tree approach for determining diagnoses of many *DSM-IV* Axis I psychiatric disorders; the SCID-II was used for making diagnoses of Axis II personality disorders. Participants receiving a psychiatric diagnosis were clinically reappraised by one of the study investigators, who also evaluated participants for suicidal ideation, thought disorder, delusions, and hallucinations. The Hopkins Symptom Checklist–Revised (SCL-90-R; Derogatis, 1983; Derogatis & Cleary, 1977) was administered at baseline and monthly to measure self-reported psychiatric distress (using a 0-4 Likert Scale) across 90-items and 9-subscales (e.g., depression, anxiety). The present study used the Global Severity Index (GSI) score, which is the average rating given to all 90 items and correlates highly to the individual scales. Finally, the Self-Report Measure of Medication Adherence (SMMA; Morisky, Green, & Levine, 1986) was administered monthly to assess adherence to prescribed psychiatric medications. The SMMA uses a 4-point Likert Scale, with lower scores indicating better adherence. Interviewers completed a comprehensive and ongoing training protocol to establish and help sustain good inter-rater reliability over the course of the study (see Kidorf et al., 2013).

Participants submitted urine samples for testing once per week using a modified random schedule (Monday, Wednesday, or Friday). Urine samples were obtained under direct observation (through a one-way mirror) and tested at a certified laboratory that employed TLC and EMIT testing for the presence of opioids, cocaine, and benzodiazepines. Alcohol use was measured monthly using self-reported number of days drinking alcohol in the past 30-days. Most participants (78%; $n = 97$) completed all three monthly assessment follow-ups, though a trend finding showed that baseline negative participants completed somewhat more follow-ups than baseline positive participants ($M = 2.76$; $SD = 0.71$ vs. $M = 2.46$; $SD = 0.92$; $t = 1.90$, $df = 123$, $p = .06$). Participants were paid $40.00 for completion of the baseline assessment battery, and $15.00 for completing each follow-up assessment.

2.3. Procedure

The present study re-analyzes data from the parent study (Kidorf et al., 2013) by classifying participants into one of two conditions based on the 4-week baseline urinalysis results: (1) no illicit drug (i.e., opioid, cocaine, sedatives) positive urine samples (baseline negative; $n = 50$) or (2) at least one illicit drug-positive urine sample (baseline positive: $n = 75$). The full study procedures of the parent study are detailed elsewhere (Kidorf et al., 2013) and are summarized here. Participants in the parent study were randomly assigned to either an attendance reinforced on-site integrated psychiatric care or a standard on-site integrated care condition that did not include the voucher-based attendance reinforcement. The only difference between these two conditions was that those receiving the attendance reinforcement had the opportunity to earn voucher-based incentives ($25.00 per week) for each week they attended all of their scheduled psychiatric sessions. Participants subsequently exchanged voucher earnings for goods and services in the community.

All participants were offered a psychiatric service schedule that included individual psychiatrist appointments (usually scheduled once every 2 weeks), individual mental health counseling sessions (once per week), and group mental health education and support sessions (once per week). The psychiatrists formulated the initial care plan that