Concurrent Cannabis Use During Treatment for Comorbid ADHD and Cocaine Dependence: Effects on Outcome

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Abstract: Cannabis is the most widely used illicit substance in the United States with especially high prevalence of use among those with psychiatric disorders. Few studies have examined the relationship between concurrent cannabis use and treatment outcome among patients receiving treatment for comorbid substance abuse and psychiatric disorders. This study investigated the effects of cannabis use on treatment retention and abstinence from cocaine among cocaine dependent patients with Attention Deficit Hyperactivity Disorder (ADHD). Cocaine dependent patients diagnosed with current ADHD (DSM-IV, N = 92) aged 25 to 51 participated in a randomized clinical trial of methylphenidate for treatment of ADHD and cocaine dependence in an outpatient setting. The majority of patients (69%) used cannabis during treatment. Results suggest that moderate/intermittent cannabis users had greater retention rates compared to abstainers and consistent users (p = .02). This study is the first to examine concurrent cannabis use in cocaine dependent patients diagnosed with ADHD.

Keywords: ADHD, cannabis, cocaine, comorbidity, treatment outcome

1. INTRODUCTION

Although cannabis is the most commonly used illicit substance in the United States, it remains among the least studied clinically (1). Cannabis
use is especially prevalent among individuals with combined psychiatric and substance use disorders, encompassing a variety of abused drugs. The high prevalence of cannabis use both among patients with cocaine dependence and among those with Attention Deficit Hyper-activity Disorder (ADHD) poses the important question of whether continued cannabis use during treatment of comorbid cocaine dependence and ADHD leads to poor treatment outcome. The question is plausible because the reinforcing and rewarding effects of cannabis are postulated to arise via cannabinoid receptor-mediated activation of the mesolimbic dopamine system, analogous to the effect of cocaine (2). Further, ADHD is thought to involve dopamine system deficits. Thus, cannabis use could worsen outcome of treatment for cocaine dependence by serving a priming function in triggering cocaine use, or leading to exposure to other drug-related cues. On the other hand, it could conceivably have a favorable effect as an agonist substitute. The literature on the impact of cannabis use on outcome of other substance dependencies is mixed. Some studies show a worsening of prognosis (3–5), while a few studies actually suggest no effect or favorable effects (6, 7). Here, we report the impact of cannabis use during treatment on the outcome of cocaine dependent patients with ADHD.

2. METHODS

2.1. Participants

All participants were volunteers in a clinical trial of outpatient treatment for cocaine dependence and ADHD, recruited to one of two university affiliated research clinics. Potential participants underwent a detailed medical and psychiatric assessment (including SCID interview). Eligible participants included those aged between 18–60 and who met DSM-IV criteria for both cocaine dependence and adult ADHD. Participants were excluded if they 1) met DSM-IV criteria for current psychiatric disorders other than ADHD that required psychiatric intervention, 2) were physiologically dependent on sedatives or alcohol, 3) exhibited suicidal or homicidal behavior within the past two years, or 4) were on any prescribed psychotropic medication.

All participants gave written informed consent before the screening and study procedures were initiated. The study was approved by the Institutional Review Boards of the New York State Psychiatric Institute, Columbia University, and the Long Island Jewish Medical Center.

2.2. Study Design

Subjects in this study participated in a 14-week placebo-controlled trial of sustained-release methylphenidate. Throughout the trial, patients visited
the clinic three times per week, providing a urine specimen at each visit. Clinical assessments of drug use and ADHD were conducted weekly. All participants received weekly individual cognitive behavioral therapy (CBT-RP) conducted by graduate-level clinical psychologists. Urine samples were tested for cocaine metabolites. Cannabis scored as positive or negative based on 100 ng/ml cut-off (≥100-positive). New cocaine use was determined with the quantified method developed by Preston et al. (8). The 92 subjects examined for this manuscript were a subset of the subjects that participated in the original medication trial (n = 106) for whom THC urine data were available.

2.3. Measures

Outcome measures examined were: 1) weeks in treatment, defined as the total number of study weeks completed (range 1–14) on which urine was collected; 2) abstinence, defined as 2 or more consecutive cocaine negative weeks at any time during the trial; and, 3) the number of new cocaine positive urine samples submitted per week (range 0–3) over the course of the study.

Cannabis use during the study was examined as a potential predictor of cocaine use outcome. Subjects were classified based on the proportion of cannabis-positive urines (# urine positive/total # urines submitted) during the 13-week follow-up into three groups as follows: cannabis abstainers (0% positive, n = 28), intermittent/moderate users (greater than 0% and up to 66% positive, n = 28), and heavy/consistent users (66%–100% positive, n = 36).

2.6. Data Analysis

Weeks retained in treatment were compared across groups using Kaplan–Meier survival curves and the log-rank statistic. The effect of gender on retention was examined by fitting a Cox regression model with cannabis status and gender and their interaction as factors in the model and was found not to be significant. Rates of abstinence from cocaine were compared across groups using the chi-square test. Longitudinal analyses were performed to examine the effect of cannabis use on cocaine use over the course of the study. We employed general estimating equations (GEE, using SAS’s PROC GENMOD) to analyze the ordinal outcome defined by the number of cocaine positive urine specimen submitted per week (range 0–3) over the course of study. We fitted a cumulative logit model with time as a linear factor and cannabis status as a 3-level categorical factor in the model. The interaction between the two factors and the main effect of gender was tested and found not to be significant.
and was removed from the model. All tests were performed at the 5% significance level. Effects of randomly assigned medication treatment were not included in this analysis.

3. RESULTS

3.1. Baseline Sample Description

Subjects (n = 92) were predominantly male (84%), white (60%), had an average age of 37 years, were single (23% were married or living with a partner), employed (87%) and had completed on average 14 years of schooling (range 8–18). Subjects were using cocaine a mean of 3 (SD = 2) days per week and $42 (SD = $51) per day of use at baseline. The cannabis use subgroups differed by gender with no females present in the intermittent/moderate use group, 25% females in the abstainer group, and 22% in the consistent group (X² = 7.93, df = 2, p = .02). No other significant differences between groups in baseline demographic or clinical features were observed.

3.2. Retention

Comparison of survival curves for the 3 levels of cannabis users reveals that abstinent and heavy/consistent cannabis users had worse treatment retention than intermittent/moderate users (see Figure 1). At week 14 retention rates were 25% among abstainers, 57% among intermittent/moderate users, and 39% among heavy/consistent users (Log-rank = 7.59, df = 2, p = .02).

3.3. Effect of Cannabis Use on Cocaine Use Outcome

Abstinence data were available for 90 subjects and of those 32% (29 out of 90) achieved 2 or more weeks of abstinence from cocaine. The 3-way stratification by cannabis use did not reveal any significant differences in cocaine abstinence rates across the groups (cannabis abstainers 26% (7 out of 27), intermittent/moderate users 39% (11 out of 28), heavy/consistent users 31% (11 out of 35); X² = 1.14, df = 2, p = .57). The logit model similarly revealed no significant effect of cannabis use group (X² = 1.97, df = 2, p = 0.37) on weekly cocaine urines.

4. DISCUSSION

A large proportion of patients used cannabis during treatment for cocaine dependence and ADHD. Cannabis use during treatment was
not associated with a worsening of cocaine use outcome in this sample. Few patients achieved cocaine abstinence, suggesting that this group of patients was difficult to treat overall. There was, however, significantly better treatment retention among intermittent/moderate cannabis users compared to abstainers and heavy/consistent users. This is consistent with previous findings in a study of opiate dependence (6), which also suggested that moderate levels of cannabis use were associated with better outcome compared to minimal use or heavy use.

All patients in this trial received manualized CBT-RP. Beneficial effects of CBT-RP have been shown to emerge and strengthen over time during post-treatment prospective follow-up (9). This is exactly the period in which we previously showed that ongoing cannabis use predicted poor outcome of cocaine dependence in a longitudinal study (10). It is possible that the during-treatment time window is too short to show an adverse effect of cannabis use on cocaine outcome, and that post-treatment follow-up is needed. Alternatively, cocaine-dependent patients with comorbid ADHD may differ from the patients followed prospectively in the previous study, many of whom had comorbid major depression. Further studies should include a post-treatment follow-up evaluation so that this question can be addressed.

Among the studies of cannabis effects on outcome during treatment for other drugs, none to our knowledge has included information on...
patients’ reasons for continued cannabis use during treatment. Given how prevalent cannabis use is in the treatment setting, a better understanding of the reasons and expectancies about cannabis use among cocaine patients, and information about the effects of cannabis among these patients may lead to insights on how to improve their treatment overall.

The results of the present study might be interpreted as a signal to clinicians that cannabis use during treatment can be ignored. We suggest that this is unwise for two main reasons. First, we do not know about post-treatment effects of the cannabis use in this population, and our previous work suggests that this is likely a significant factor. Second, ignoring cannabis use sends mixed signals to patients about the clinician’s attitude towards the use of illegal drugs and associated activities.

The findings suggest that future medication development efforts should consider medication acting at the cannabinoid receptors levels, possibly as partial agonist.

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