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Substance Use Predictors of Poor Medication Adherence: The Role of Substance Use Coping Among HIV-Infected Patients in Opioid Dependence Treatment

Adam Gonzalez,
Department of Psychiatry, Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA; Department of Psychiatry and Behavioral Science, State University of New York, Putnam Hall-South Campus, Stony Brook, NY 11794, USA

Matthew J. Mimiaga,
Department of Psychiatry, Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA; The Fenway Institute, Boston, MA, US

Jared Israel,
Department of Psychology, University of Missouri, St. Louis, MO, USA

C. Andres Bedoya, and
Department of Psychiatry, Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA

Steven A. Safren
Department of Psychiatry, Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA;The Fenway Institute, Boston, MA, USA

Abstract

Many HIV-infected injection drug users (IDUs) continue to use illicit substances despite being in substance use treatment. Substance use is associated with non-adherence to HIV medications; however underlying mechanisms regarding this relation are understudied. The current investigation examined the role of substance use coping in terms of the relation between substance use and HIV medication adherence. Participants were 121 HIV-infected IDUs (41 % female, *M* age = 47, SD = 7.1) in opioid dependence treatment. Participants completed self-report questionnaires, were administered clinical interviews and oral toxicology screens, and used a medication-event-monitoring-system cap to assess 2 week HIV medication adherence. The use of cocaine and multiple substances were significantly related to decreased medication adherence. Substance use coping mediated these associations. Findings highlight the importance of assessing, monitoring, and targeting ongoing substance use, and ways to increase positive coping for HIV-infected IDUs in substance use treatment to aid in HIV medication adherence.

Keywords

HIV/AIDS; Medication adherence; Substance use; Coping; Cocaine

Correspondence to: Adam Gonzalez.
adam.gonzalez@stonybrook.edu.

Introduction

HIV medication adherence is a vital component of successful viral suppression, delays in clinical progression, and decreased AIDS-related deaths [1-4]. In addition, adherence is necessary for decreasing risk for developing drug resistance to certain antiretroviral therapies (ART) [5, 6]. Moreover, ART adherence may have important secondary HIV prevention implications. For example, research with heterosexual couples [7-9] and men who have sex with men (MSM) [10] suggest that effective use of ART may reduce the likelihood of sexual transmission of the virus.

There is a growing body of research examining factors that may impede effective ART adherence. Across studies, substance use is one of the most consistent barriers to HIV medication adherence (see for review [11]). Use of injected drugs, in particular, is related to ART non-adherence [12,13], even in the context of receiving treatment for substance abuse [14, 15]. In addition, there is some evidence to suggest that use of different drugs may impact adherence and ART effectiveness differently [11, 16]. For example, use of stimulants versus non-stimulants results in different rates of adherence [17]. Nevertheless, among HIV-infected IDUs, continued drug use stands out as one factor that maintains medication adherence difficulties [13, 14]; however, the types of drugs used and mechanisms by which ongoing use is related to adherence difficulties are understudied.

Self-regulation and coping theories of substance use indicate that individuals may engage in substance use behavior because they believe it can help them cope with negative life events and/or dysregulated emotional states [18,19]. To the extent that life stress and/or negative affective states (e.g., depression) [20] and substance use [11] interfere with medication adherence, individuals with HIV who use substances to cope may be at increased risk for HIV medication non-adherence. Substance use coping, in addition to other life stressors that can accompany substance abuse (e.g., homelessness) [21], might contribute to greater degrees of dysregulation, resulting in adherence difficulties [22].

The current study sought to examine

1. The type of substances used by HIV-infected IDUs who were in substance abuse treatment.
2. Which substances were related to worse ART adherence.
3. Whether one possible mechanism, substance use coping, would mediate the relation between substance use and medication non-adherence.

Methods

Participants

Participants were 121 adults (41 % female; *M* age = 47.00; SD = 7.1) with HIV in treatment for opioid dependence (e.g., medication-based and/or individual/group therapy), and screened for participation in a treatment study of depression and HIV medication adherence in HIV-infected IDUs. Participants' race/ethnicity was 45 % White, 31 % Black, 20 % Other, 2 % Native American, and 1 % Native Hawaiian/Pacific Islander. In addition, 28.2 % identified as Hispanic. On average, participants reported 11 years (SD = 3.0) of educational attainment and a CD4 T cell count of 431 (SD = 250.7). More than half (61.2 %) of the sample had an undetectable viral load. The majority (79 %) of the sample reported using at least one substance within the past 30 days. Specific substances used include: opiates (41 %), cocaine (37 %), sedatives (36 %), alcohol (22 %), and marijuana (19 %); 48 % reported using two or more of these substances. The average 2 week HIV medication adherence for the sample was 68 % (SD = 27.71).

Measures

Demographics—Demographic information (gender, age, educational attainment) were self-reported. We tested for HIV viral load and CD4 T cell count at the baseline visit; although if participants had recent tests completed by their infectious disease clinic (in the past month), they were obtained from medical records.

Recent Substance Use—The Addiction Severity Index-Lite (ASI-Lite) [23] and oral toxicology screening were used to assess use of opiates, cocaine, sedatives, alcohol, marijuana, and multiple substances (use of two or more substances during the same day) within the past 30 days. The ASI-Lite assesses alcohol and drug use in the past 30 days, lifetime problematic use, methods of drug administration, and whether the substance was prescribed. Results of toxicology reports (positive vs. negative for use of each substance) and self-reported substance use via the ASI-Lite were combined to assess specific drug use within the past 30 days and dichotomous (use vs. no use) substance use variables were created. Substance use was marked positive if the participant either had a positive toxicology screen or self-reported using a specific substance. In addition, a dichotomous multiple substance use variable was created to account for overlap in use of different substances. The use of opioid agonists (e.g., methadone) was excluded from the opioid use variable as study participation required some form of substance use treatment for enrollment, including methadone maintenance therapy. Participants were also informed that their responses about substance use would be kept confidential and not reported to either their substance abuse treatment provider or facility.

Assessment of ART Adherence—Medication-event-monitoring-system (MEMS) caps (AARDEX) were used to assess 2 week HIV medication adherence. MEMS caps recorded each instance of bottle opening, monitoring the antiretroviral medication that the participants considered the most difficult to remember or the dose taken most frequently. Doses that participants may have taken without opening the pill cap (e.g., took out afternoon doses when they opened the pill bottle in the morning) were counted as taken if participants could recall specific instances when they took their medications but did not use the cap. A dose was considered missed if it was not taken within a 2 h window of the designated time. The final adherence percentage represents the percent of doses taken on-time over the 2 week period, corrected for times when participants took the medication but did not use the MEMS cap. These procedures, including using a 2 week monitoring period are common for measuring HIV medication adherence [23-28].

Substance Use Coping—The substance use coping subscale of the Brief COPE [29] was used as a potential mediator (e.g., “I have been using alcohol or drugs to make myself feel better”). The Brief COPE assesses 14 different strategies to cope with stress from the larger COPE inventory, with each subscale consisting of two items. The Brief COPE has been previously used successfully to assess coping strategies among persons with HIV [30, 31]. The substance use coping subscale has demonstrated excellent internal consistency in previous samples (Cronbach’s α = .90) [30] and in the current sample (Cronbach’s α = .91).

Procedure

Participants were recruited from methadone clinics in the greater Boston area and through community outreach and hospital-based HIV clinics. Although individuals were recruited for a study of depression and adherence to HIV medications in IDUs, we screened all HIV-infected IDUs who were in substance abuse treatment regardless if they self-reported having problems with medication adherence. Interested persons completed a baseline assessment over two study visits that consisted of informed consent procedures, administration of an assessment battery that included a clinical psychiatric interview, an oral toxicology screen,

self-report questionnaires, and blood-draw. Participants were then given a MEMS cap, to monitor their HIV medication adherence for a 2 week period, which they returned at the second study visit prior to randomization into one of the two study arms. Participants were compensated $50 for their time and participation.

Participants were eligible if they were age 18 or older, HIV-seropositive, prescribed antiretroviral therapy for HIV, endorsed a history of injection drug use, and were enrolled in current opioid treatment for at least one month. Individuals were excluded if they endorsed criteria for any active untreated, unstable, major mental illness (e.g., mania or psychosis), inability or unwillingness to provide informed consent, or had current participation in CBT for depression. Data for the current analyses were collected from all participants completing baseline procedures for the larger study prior to treatment randomization and initiation (see [27]).

Data Analytic Strategy

Descriptive statistics were first examined for demographic and substance use variables. A series of hierarchical regression analyses were conducted with percentage of 2 week HIV medication adherence as the criterion variable. At step 1 of each model, the main effects of gender, age, and number of years of education were entered. These covariates were chosen on an a priori basis because previous work indicates significant relations with ART adherence [32-35]. At step 2, a dichotomous variable of past 30 days use for specific substances [opiates, cocaine, sedatives, alcohol, marijuana, and multiple substances (use of two or more substances)] was entered. For this variable we included those who either self-reported illicit substance use on the ASI-Lite or who screened positive on the toxicology screen. For substances that were significantly related to medication non-adherence, hierarchical regression procedures as described by Baron and Kenny [36] and Sobel tests [37] were conducted to test the hypothesis that using substances to cope would mediate the relationship between substance use and medication non-adherence.

Results

Hierarchical regression analyses indicated that at step 1 (covariates), only gender was significantly related to medication adherence ($\beta = -.22$, $p = .02$) with men reporting higher rates of adherence than women ($M = 73.59$, SD = 25.76 and $M = 59.62$, SD = 28.56; respectively). At step 2 of the models, only cocaine ($\beta = -.22$; $p = .02$) and multiple substance use ($\beta = -.22$; $p = .02$) within the past 30 days were significantly related to decreased HIV medication adherence (criterion variable). There was also a non-significant trend for opiate use ($\beta = -.17$; $p = .07$) in terms of decreased adherence.

A second set of hierarchical regression analyses were conducted to test the relations between cocaine, multiple substance use (predictors) and substance use coping (the mediator). At step 1, gender, age, and number of years of education were entered as covariates. At step 2, the dichotomous cocaine or multiple substance use predictor variable was entered. The overall models accounted for 24 % (cocaine as predictor) and 25 % (multiple substances as predictor) of variance in substance use coping. Control variables at step 1 did not account for a significant portion of variance. At step 2 of the models, cocaine ($\beta = .44$; $p < .001$) and multiple substance use ($\beta = .47$; $p < .001$) accounted for an additional 19 and 21 % of variance, respectively.

A third set of hierarchical regression analyses were conducted to test the relations between substance use coping (the mediator) and HIV medication adherence (criterion variable). The overall model accounted for 12 % of variance in medication adherence. Control variables (gender, age, and number of years of education) entered at step 1 did not account for a

significant portion of variance. At step 2, substance use coping ($\beta = -.30$; $p = .004$) accounted for an additional 8 % of variance.

Finally, a set of hierarchical regression analyses were conducted to test the meditational role of substance use coping in the relation between cocaine, multiple substance use and medication adherence. In these models, when controlling for cocaine and multiple substance use, respectively, substance use coping was significantly related to medication adherence; however, cocaine and multiplesubstance use, respectively, were no longer significantly related to medication adherence. Thus, substance use coping significantly mediated the relation between cocaine, multiple substance use and medication adherence (above and beyond effects due to gender, age, and education; see final model in Table 1). Post hoc analyses using the Sobel test for mediation confirmed that substance use coping fully mediated the relation between cocaine, multiple substance use and medication adherence ($Z = -2.65$, $p < .01$ and $Z = -2.65$, $p < .01$; respectively).

Discussion

The current investigation examined the mediating role of substance use coping in the relationship between substance use and HIV medication adherence among HIV-infected IDUs in treatment for opioid dependence. There are three key findings from the present data. First, many HIV-infected IDUs continue to use various substances while in opioid dependence treatment; with the most common substance being opiates (36 %), and the second most common being cocaine (33 %). Second, use of cocaine and multiple substances were significantly related to decreased HIV medication adherence for this population above and beyond demographic characteristics. Last, using substances as a way of coping with stress significantly mediated the relation between cocaine, multiple substance use, and medication non-adherence after accounting for potential covariates.

The current findings highlight the significance of incorporating continued substance use screening in the context of substance use treatment and the importance of using interventions to help promote more positive coping strategies among HIV-infected IDUs in this context. Indeed, previous work suggests that identifying and addressing ongoing substance use may aid in ART and substance use treatment adherence [12, 38]. In addition, research among people without HIV suggests that using substances specifically to help regulate one's affect is related to greater anxiety and depression [39, 40], which among persons with HIV may lead to greater HIV medication adherence problems [41]. Thus, although individuals may engage in substance use because they believe it will help them manage dysregulated mood states, using substances actually perpetuates both negative mood and may elicit poor health behaviors (e.g., medication non-adherence). To this end, understanding reasons for substance use (recreational vs. coping) may aid in designing substance cessation and adherence interventions.

There are several notable limitations of the present investigation. First, toxicology screens were used to identify recent substance use behavior in conjunction with retrospective self-report of use in the past 30 days. Future work would benefit from assessing real-time substance use behaviors via ecological momentary assessment techniques [42] or random toxicology assessments to more accurately capture relations between ongoing substance use and ART adherence. In addition, it would be important to examine the effects of severity of use (frequency and quantity vs. any use). Second, individuals were participating in different types of opioid abstinence treatments, which may have differentially impacted substance use behavior. In addition, other aspects of the sample may have impacted the findings including the fact that all participants were being recruited for a study focused on depression and medication adherence and more than half (61 %) had an undetectable viral load. Thus, the

current results may not be generalizable to all HIV-infected IDUs in substance abuse treatment. Future investigations might examine the relationship among substance use relapse and ART adherence within the context of a structured substance use treatment or account for variations in addiction treatment modalities. Third, the final meditational models accounted for a relatively small portion of variance in adherence (14 % cocaine and 15 % multiple substance use). As such, there are likely other clinically relevant psychosocial stressors that may have affected rates of ART adherence [43]. For example, among HIV-infected IDUs, life stressors (e.g., homelessness) significantly impact adherence [21, 44]. In addition, there may be underlying difficulties with emotion regulation that might help explain the effects of substance use coping on adherence. Future work is needed to better understand different vulnerability factors for adherence difficulties, in addition to ongoing substance use behavior among HIV-infected IDUs. Last, of those who were using multiple substances, 60 % were using cocaine. Future work is needed to assess whether cocaine use is uniquely related to medication adherence problems regardless of using other (i.e., multiple) substances.

The present data and previous research [17, 45] under-score the negative effects of cocaine use, in particular, in relation to medication non-adherence. Additionally, other work suggests that cocaine use is related to HIV disease progression, specifically, low CD4 T cell count and elevated HIV viral load independent of ART adherence [46,47]. Thus, identifying and treating cocaine use may have important disease management implications (independent of ART adherence). There may be aspects of cocaine use, specifically the withdrawal process (e.g., concentration problems, intense cravings) that might help explain difficulties with medication adherence; however, future research is needed to investigate specific drug and withdrawal effects in terms of ART adherence. Comprehensive interventions addressing use of cocaine, multiple substances, medication non-adherence, and coping skills training are warranted for HIV-infected IDUs actively receiving addiction treatment. Future work would benefit from developing, testing, and disseminating substance use treatments that involve affect management and coping skills training components to aid in effective sustained sobriety and HIV disease management.

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Table 1

Substance use coping mediating the relations between cocaine, multiple substance use and HIV medication adherence

Dependent variable: Adherence[a]	R^2	β	p
Final Model 1	.14		
Gender[b]		−.22	.03
Age		−.06	.57
Education[c]		−.12	.28
Cocaine use[d]		−.09	.40
Substance use coping[e]		−.26	.02
Final Model 2	.15		
Gender		−.25	.02
Age		−.08	.42
Education		−.11	.29
Multiple substance use[d]		−.15	.20
Substance use coping		−.24	.04

[a] MEMS past 2 week ART adherence

[b] Gender coded as 1 = male, 2 = female

[c] Years of education

[d] Substance use in past 30 days indexed by ASI−Lite [48] and oral toxicology screening coded as 0 = no use, 1 = use

[e] Brief COPE [29]