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Marijuana use and HIV treatment outcomes among PWH receiving care at an Urban HIV Clinic

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Abstract

Background—While marijuana use is prevalent among persons with HIV (PWH), few studies have examined the relationship between marijuana use and HIV treatment outcomes independent of alcohol and other drug use.

Methods—We conducted a prospective cohort study to examine the relationships between frequency of marijuana use and antiretroviral therapy (ART) adherence and viral suppression in patients enrolled in the Johns Hopkins HIV Clinical Cohort between September 2013 through

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November 2015 (N=1377). We categorized marijuana use as no use, none in the last 3 months, monthly use or less, weekly/daily. Our outcomes of interest were use of ART, 90 ART adherence, and viral suppression (HIV1-RNA <200 copies). We conducted multivariable analyses to examine associations between the frequency of marijuana use and our treatment outcomes, using generalized estimating equations to account for repeated measures. Other independent variables of interest included alcohol use, other drug use, and depressive symptoms. Analyses were adjusted for age, race, sex and HIV acquisition risk factor.

Results—In multivariable analyses we found no statistically significant association between frequency of marijuana use and our treatment outcomes. Alcohol use, other drug use and depressive symptoms were associated with lower odds of ART adherence and viral suppression.

Conclusions—In this sample of PWH in care, frequency of marijuana use independent of other substance use does not appear to be associated with negative HIV treatment outcomes. Our results indicate that unlike alcohol, other substances and depression, marijuana use may not be a barrier to the effective treatment of HIV.

Keywords

HIV; Marijuana; Adherence; Viral Suppression

1. Introduction

Alcohol and other drug use are prevalent among persons living with HIV (PWH) and are barriers to optimal use of antiretroviral therapy (ART) and viral suppression [1–2]. Hazardous alcohol and drug use contribute to HIV disease progression both by reducing adherence to ART and by accelerating disease progression [1–5]. Marijuana use is generally included in studies assessing drugs as a barrier to HIV treatment adherence, though relatively fewer studies have evaluated the specific relationship between marijuana use and adherence to HIV treatment and disease progression independent of alcohol and other drug use.

Marijuana is the most commonly used illicit drug in the United States. In 2014, 8.4% of persons aged 12 years and older reported marijuana use during the past month and 13.2% reported use during the past year [6]. Recent reports suggest that marijuana use is even more widespread among PWH [7–8]. A multicenter cohort of HIV infected patients receiving care in 8 US cities between 2013–2015 found 31.6% of patients reported marijuana use during the past 3 months [9]. In a recent Florida sample of PWH in care, 20% reported recent marijuana use with 7% reporting daily use [10]. With these elevated levels of marijuana use among PWH receiving care, there is need to better characterize the relationship between marijuana use and HIV treatment outcomes, controlling for the frequent comorbidity with alcohol and other illicit drug use.

Studies of marijuana use and HIV outcomes have spanned from a time of older, more complicated ART regimens to the current simpler and less toxic era of ART. Studies also have varied in examining marijuana use for symptom management versus illicit, recreational use and, as a result, results have been inconsistent. While some studies have found a positive

association between marijuana use and ART adherence [11–13], others have found that frequency [14] and severity of marijuana use (e.g. having marijuana dependence/marijuana use disorder (MUD)) [15] are associated with worse ART adherence. In contrast, a recent study of illicit drug users with HIV found no association between daily marijuana use and optimal treatment adherence [16].

Similarly, studies of marijuana use and HIV-RNA suppression have also yielded mixed findings. In one study cannabis dependent patients were more likely to have significantly lower recent adherence and higher viral load than nondependent users or non-users, although these effects were mitigated by age, education and alcohol consumption [15]. Others have found no significant association between marijuana use and viral suppression [4, 10]. The inconsistency of findings across studies highlights the need for further evaluation of these relationships in larger, mixed sex samples.

The present study aims to examine the relationships between marijuana use and treatment adherence and viral suppression in a large cohort of HIV infected individuals engaged in care at an urban center. We hypothesize that 1) ART use will not differ as a function of marijuana use 2.) More frequent marijuana use (independent of alcohol and other drug use) will be associated with lower adherence to ART and higher viral load.

2. Methods

2.1 Study Design

This is a prospective cohort study of individuals enrolled in the Johns Hopkins HIV Clinical Cohort (JHHCC), a longitudinal clinical cohort of PWH receiving care in the Johns Hopkins HIV Clinic. All individuals entering into care in the clinic are eligible to participate. Demographic, clinical, laboratory and pharmacy data are retrieved both by trained staff (medical record data) and electronically (laboratory/pharmacy data) at 6 month intervals. In addition, the JHHCC collects patient self-report of alcohol, opioid, cocaine, marijuana and other drug use, antiretroviral therapy (ART) use and ART adherence, and depressive symptoms at approximately 6-month intervals using a tablet-based computer assisted interview (CASI). This survey takes approximately 15 minutes to complete. Responses to these items are confidential and not shared with the participant's provider. A detailed description of the data collection procedures of the JHHCC is available elsewhere [17].

In September 2013, questions were added to the CASI that queried frequency of marijuana use, thus determining the start date of this study. We included all PWH enrolled in the JHHCC who participated in the CASI from September 2013 through November 2015 (N=1377). For analyses related to ART adherence, we included only those individuals on ART, and for those examining viral suppression, we only included individuals on ART and with an HIV-RNA result within 6 months of the CASI. The median number of interviews per person was 2, with a minimum of 1 and a maximum of 7 (n=1). There were a total of 3179 interviews.

Written informed consent is obtained from the participants. The JHHCC is approved by the Johns Hopkins University School of Medicine's Institutional Review Board.

2.2 Independent Variables

Our primary independent variable was frequency of marijuana use. This was assessed using the National Institute on Drug Abuse Modified Alcohol Smoking and Substance Involvement Screening Test (NIDA ASSIST) [18] questions 1) “In your life, have you ever used marijuana? And if yes, 2) “In the past three months, how often have you used marijuana?” with the following response options: “Never, Once or Twice, Monthly, Weekly, Daily or Almost Daily.” This variable was collapsed into 4 categories: 1) no lifetime use 2) past use, but none in the past 3 months 3) monthly or less 4) weekly or daily/almost daily.

Other independent variables, including alcohol use, other substance use, and depressive symptoms were chosen a priori based on literature demonstrating associations with HIV outcomes. We assessed alcohol frequency, using the first question of the Alcohol Use Disorders Identification Test (AUDIT) [19], “How often do you have a drink containing alcohol?” with response options: “Never, Monthly or less, 2–4 times per month, 2 to 3 times per week, 4 or more times per week” [20]. We assessed lifetime and past three months use of cocaine and heroin using the NIDA ASSIST and collapsed use into the following categories: no lifetime heroin or cocaine use, past heroin or cocaine use, current heroin or cocaine use. Depressive symptoms were measured using the Patient Health Questionnaire-8 (PHQ-8) and were included as a continuous variable [21]. Other variables including sex, age at the time of the interview, race, and HIV acquisition risk factor were obtained from clinical records. Sex was categorized as female, male-MSW, male-MSM. CD4 cell count (closest to the time of the interview) was obtained from the laboratory file.

2.3 Dependent Variables

Antiretroviral therapy (ART) use was determined by self-report on the CASI, which asked whether an individual was currently taking ART. ART adherence was collected using a visual analog scale that asked participants to mark the point on the line (between 0 and 100 %) that reflected how much of their HIV medication they had taken in the last month [22]. Self-reported adherence of <90% was classified as non-adherence [23]. HIV-1 RNA was obtained from laboratory records; viral suppression was defined as an HIV-1 RNA of <200 copies/mL. HIV-1 RNAs were included if drawn either on the date of the interview, or within 6 months subsequent to the interview. If multiple HIV-1 RNA tests were drawn during this period, we used the test closest to the date of the interview.

2.4 Statistical Methods

Descriptive statistics were calculated for the overall cohort and for each marijuana use group. We used generalized estimating equations (GEE) to account for the correlation structure created by the use of multiple measurements on each individual [24]. These methods were applied to each of the dichotomous outcomes (ART use, adherence, and viral suppression) in separate models using logit link and an exchangeable correlation matrix. We adjusted our models for age, race/ethnicity, sex, heroin and cocaine use, alcohol frequency, depressive symptoms, and enrolment time (time enrolled in the clinic). Sex and race/ethnicity were fixed variables. All other predictors including marijuana, alcohol and drug use, and depressive symptoms, were captured at each interview and thus varied across visits. Using the categorical variables for marijuana, alcohol and heroin/cocaine described above,

we also tested the interaction of 1) marijuana frequency and alcohol frequency and 2) marijuana frequency and heroin and/or cocaine use on our three outcomes. The interaction terms were entered into multivariable models. The data were analyzed using STATA, version 13.0 (StataCorp, College Station, TX, USA)

3. Results

3.1 Baseline Characteristics as a Function of the Frequency of Marijuana Use

Table 1 displays baseline characteristics of the overall study population and each marijuana use group. The average patient age was 51 years old. The majority of patients were African American (84%) and male (62.2%). Half of our study population (51.7%) reported having used marijuana at least once in their lifetime, 20% reported marijuana use in the prior three months and nearly 10% of the entire sample reported weekly (3.6%) or daily use (6.2%). Of those who used marijuana in the prior three months ($n=277$) 49% reported weekly/daily use (18% weekly use 31% daily use), and 51% used monthly or less. Increased frequency of current marijuana use was associated with younger age, more frequent use of alcohol, use of other drugs (heroin/cocaine) and higher score on the PHQ-8.

3.2 Use of Antiretroviral Therapy

Overall, 91% of participants were on ART at baseline, and 93% of CASIs were conducted while participants reported being on ART. Table 2 displays the relationship between frequency of marijuana use and ART use, ART adherence, and HIV-1 RNA viral suppression (among those on ART). After adjustment for sex, age, race, depressive symptoms, alcohol, cocaine/heroin use and clinic enrollment time, marijuana use at any frequency was not associated with use of ART. In the multivariable model, increased frequency of alcohol use remained significantly associated with decreased use of ART (Monthly, AOR: 0.67, 95% CI: 0.47–0.96, 2–4 times per month, AOR: 0.48, 95% CI: 0.31–0.76, 2+ times per week, AOR: 0.61, 95% CI 0.39–0.97), as did current heroin and/or cocaine use (AOR: 0.35, 95% CI: 0.23–0.55). There was no interaction between marijuana and alcohol use nor marijuana and heroin/cocaine use on use of ART.

3.3 Antiretroviral Adherence

Overall, 92% of participants on ART reported >90% adherence at the time of the first included interview, and on 92% of CASIs overall. In bivariable and multivariable analyses there was no statistically significant association between marijuana use and adherence to antiretroviral therapy. In multivariable analysis, alcohol use two or more times a week (AOR=0.52, 95% CI=0.34–0.79) was associated with decreased adherence. Past and current heroin/cocaine use (past use, AOR=0.58, 95% CI=0.40–0.83; current use: AOR=0.30, CI=0.19–0.47) and depressive symptoms (AOR=0.93, 95% CI=0.90–0.96) were also associated with decreased adherence. There was no interaction between marijuana and alcohol use and marijuana or heroin/cocaine use on ART adherence.

3.4 HIV-1 Viral Load Suppression

Overall 89% of participants had an undetectable viral load at their first included interview, and 88% of tests during the study period were undetectable. In multivariable analysis past

marijuana use, compared to none was associated with an increased odds of viral suppression (AOR: 1.45, 95% CI: 1.07–1.96). There was no association between monthly or daily marijuana use and viral suppression. Past heroin/cocaine was negatively associated with viral suppression while neither current heroin/cocaine use nor alcohol use were associated with viral suppression. Increasing depressive symptoms, however, were associated lower viral load suppression (OR=0.96, 95% CI=0.93–0.99). There was no interaction between marijuana and alcohol use nor marijuana and heroin/cocaine use on viral suppression.

4. Discussion

In our study of PWH receiving care in an urban setting we found that self-reported marijuana use was not associated with use of ART, ART adherence, or viral suppression. In contrast, alcohol use and heroin/cocaine use were associated with lower use of ART and poorer ART adherence. Depressive symptoms were associated with lower ART adherence and lower viral suppression. Our findings suggest that in our sample of urban men and women engaged in care during the current ART era, marijuana use does not appear to be associated with negative HIV outcomes.

In prior literature, the relationship between marijuana use and HIV treatment outcomes seems to have varied based on whether marijuana was used for symptom management versus recreational or illicit use. Early studies found a positive association between marijuana use and improved ART adherence [11–13]. These studies, which focused on marijuana use for symptom control, were conducted in an earlier, more complicated era of ART therapy, with greater medication side effects and more severe HIV disease related symptoms. These studies reported that patients had higher rates of adherence to ART therapy when using marijuana for management of nausea and other symptoms. In contrast, other studies have found a negative relationship between marijuana use and ART adherence [14, 15]. In these studies, frequent or dependent marijuana use was associated with decreased medication adherence. An early study, conducted Wilson et al (2004), at a time where there were limited options for once daily dosing, stratified patients by frequency of marijuana use and found patients who smoked more than 4 times a week were less likely to be adherent to their ART regimen [14]. Similarly, in a smaller convenience sample of 180 PWH patients, Bonn-Miller et al compared persons who were cannabis dependent, cannabis users and nonusers [15]. They found that persons with cannabis dependence were less adherent both by pill count and self-report; however, differences in self-reported adherence were no longer observed when analyses were controlled for age, education and alcohol consumption. Consistent with our results, a recent longitudinal cohort study of illicit drug users with HIV in Vancouver found no association between daily marijuana use and treatment adherence in multivariable analysis [16]. Similarly, in a recent analysis of a Florida cohort of PWH, no relationship between marijuana use and HIV outcomes was observed [10]. It is important to emphasize that, like the other two, very recent negative studies, our sample includes individuals in care at a time with simpler, less toxic ART regimens which may in part account for their good treatment outcomes.

We did find that alcohol, heroin/cocaine use and depressive symptoms were all associated with worse HIV treatment outcomes. This is consistent with the literature, which has

demonstrated alcohol and other drug use as well as depressive symptoms to be associated with poor initiation of ART and poor ART adherence, as seen in our study [7, 25–29]. Prior studies have also found a negative association between substance use and viral suppression [4, 30]. For example, Baum et al (2009) found that crack cocaine use decreased viral suppression despite ART adherence. We did not observe a relationship between cocaine and/or heroin use and viral suppression perhaps because our study was conducted during a time of simpler, more durable ART regimens that allows for slightly lower rates of adherence for adequate viral suppression.

4.1 Strengths

There are several strengths to this study. First, it is based on a large sample of PWH engaged in HIV treatment in the current ART era. Second, because other substance use and mental health symptoms were measured concurrently, it allows us to examine marijuana use while controlling for these other problems. Alcohol, other drug use and depression have a high rate of comorbidity with marijuana use, and have been shown previously to affect HIV treatment outcomes and thus optimal engagement in the HIV care continuum [29–33].

4.2 Limitations

There are several limitations to this study. We are unable to infer causality from our results. Additionally, marijuana use as well as other data were based on self-report, which may introduce recall bias. Also, recreational use of marijuana is illegal in the state of Maryland. As a result, marijuana use may have been underreported in this study. However, the fact that we observed the expected relationships between alcohol and other drug use and HIV outcomes suggests that patients were fairly accurate in their self-reported marijuana use. We had no measure for severity of marijuana use, including cannabis use (CUD) disorder, which based on prior literature may have a significant relationship with HIV treatment outcomes. Within our population of frequent marijuana users there is likely a subset who would be classified as having a CUD. It is possible that this subset of patients may have worse HIV outcomes, but we are unable to examine this. Finally, our sample was a largely older, urban sample, engaged in care primarily on ART with viral suppression. Thus our results may not generalize to those persons not in care, to other HIV clinic populations with a different patient mix, or to states with legalized marijuana where the prevalence of use may be higher and the frequency of use greater.

4.3 Implications and Conclusions

Despite these limitations, our study has important implications for the treatment of PWH. Our findings are consistent with other studies that demonstrate that among urban patients engaged in HIV care, marijuana use does not appear to have an effect on HIV treatment outcomes, when analyses are controlled for other commonly comorbid problems. While marijuana use may have other deleterious effects, it did not appear to independently effect ART adherence or viral suppression. It is important to note, however, that despite the availability and use of less complicated and more durable ART, alcohol use, heroin and/or cocaine use, and depressive symptoms continue to be associated with poorer HIV outcomes. These findings reinforce the need to screen for and address substance use and mental health disorders among individuals in care to optimize HIV treatment outcomes.

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Highlights

- Marijuana use is prevalent in an urban sample of PLWH
- Marijuana use, independent of other substance use, does not appear to be associated with worse HIV treatment outcomes among this sample engaged in care
- Alcohol, other drug use, and depressive symptoms are negatively associated with poorer HIV treatment outcomes

Table 1
Baseline Characteristics as a Function of the Frequency of Marijuana Use (n=1377)

Characteristics	Total Population (n=1377)	Never user (n=665)	Not in the Last 3 Months (n=435)	Monthly or Less (n=143)	Weekly/Daily (n=134)	P-Value
Mean Age, year (sd)	51.5 (10.1)	52.2 (10.8)	52.4 (8.0)	50.1 (9.4)	46.8 (11.8)	<.001
Sex, n (%)						0.007
Female	520 (37.8%)	260 (39.1%)	160 (36.8%)	62 (43.4%)	38 (28.4%)	
Male-MSW	551 (40.0%)	266 (40.0%)	188 (43.2%)	46 (32.2%)	51 (38.1%)	
Male-MSM	306 (22.2%)	139 (20.9%)	87 (20.0%)	35 (24.5%)	45 (33.5%)	
HIV Risk, n (%)						0.02
Het	525 (38.2%)	271 (40.8%)	153 (42.7%)	53 (37.1%)	48 (35.8%)	
IDU	490 (35.6%)	218(32.7%)	185 (16.5%)	51 (35.7%)	36 (26.9%)	
MSM/BI	264 (19.2%)	121(18.2%)	72 (16.5%)	31 (21.7%)	40 (29.9%)	
Other	98 (7.1%)	55 (0.8%)	25 (0.9%)	8 (0.7%)	10(1.5%)	
Race, n (%)						<.001
African American	1156 (84.0%)	561 (84.4%)	366 (84.1%)	123 (86.0%)	106 (79.1%)	
Caucasian	182 (13.2%)	73 (11.0%)	66 (15.2%)	18 (12.6%)	25 (18.7%)	
Other	39 (2.8%)	31 (4.7%)	3 (0.7%)	2 (1.4%)	3 (2.2%)	
Alcohol Use, n (%) [*]						<.001
Never	815 (59.5%)	470 (71.0%)	248 (57.3%)	43 (30.1%)	54 (40.3%)	
Monthly or less	257 (18.7%)	112 (16.9%)	81 (18.6%)	31 (21.7%)	33 (24.6%)	
2-4 times per month	134(9.8%)	36 (5.4%)	45 (10.7%)	32 (22.4%)	21 (15.7%)	
2+ times per week	165 (12.0%)	44 (6.6%)	58 (13.5%)	37 (25.9%)	26 (19.4%)	
Heroin/Cocaine Use, n (%) ^{**}						<.001
Never use	691 (50.4%)	463 (69.6%)	113 (26.1%)	51 (35.9%)	64 (47.8%)	
Past user	540 (39.4%)	161 (24.3%)	283 (65.4%)	45 (31.7%)	51 (38.1%)	
Current user	141 (10.3%)	39 (5.9%)	37 (8.6%)	46 (32.4%)	19 (14.2%)	
Depressive symptoms, phq-8 median [IQR]	1.00 [0.00, 4.00]	0.00 [0.00, 1.00]	2.00 [0.00, 5.00]	2.00 [0.00, 6.00]	3.00 [1.00,7.00]	<.001
CD4 Count, mean (sd)	549.84 (325.90)	539.85 (339.32)	567.03 (309.48)	544.06 (311.58)	547.83 (328.27)	0.609

* n=1371 at time of first included ACASI

ACASI included first time at 1372-n

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Table 2

Bivariable and Multivariable Analyses of the Relationship Between Frequency of Marijuana use and Alcohol Use, Current Heroin/Cocaine Use and Depressive Symptoms on HIV Treatment Outcomes

Variable	Outcomes					
	Use of Antiretroviral Therapy (N=1377, 3197 interviews)		Adherent to Antiretroviral Therapy (N=1312, 2986 interviews)		Undetectable Viral Load on Antiretroviral Therapy (N=1313, 2991 interviews)***	
	Bivariate Odds Ratio [95% CI]	Multivariable** Odds Ratio [95% CI]	Bivariate Odds Ratio [95% CI]	Multivariable** Odds Ratio [95% CI]	Bivariate Odds Ratio [95% CI]	Multivariable** Odds Ratio [95% CI]
Marijuana use						
Never	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
Not in the last 3 months	0.99 [0.73–1.37]	1.16 [0.82–1.65]	0.77 [0.56–1.06]	1.14 [0.80–1.63]	1.29 [0.99–1.68]	1.45 [1.07–1.96]*
Monthly or less	0.89 [0.55–1.43]	1.54 [0.94–2.54]	0.44 [0.29–0.67]*	0.90 [0.56–1.43]	0.76 [0.53–1.09]	0.95 [0.64–1.42]
Weekly/daily	1.12 [0.66–1.93]	1.73 [0.97–3.09]	0.76 [0.46–1.25]	1.31 [0.77–2.26]	0.92 [0.61–1.39]	1.19 [0.76–1.86]
Alcohol Use						
Never	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
Monthly or less	0.61 [0.43–0.87]*	0.67 [0.47–0.96]*	0.73 [0.50–1.05]	0.88 [0.60–1.30]	0.86 [0.64–1.15]	0.95 [0.70–1.30]
2–4 times per month	0.46 [0.30–0.71]*	0.48 [0.31–0.76]*	0.59 [0.37–0.94]*	0.69 [0.42–1.13]	0.74 [0.51–1.10]	0.820 [0.54–1.25]
2+ times per week	0.54 [0.35–0.83]*	0.61 [0.39–0.97]*	0.37 [0.25–0.55]*	0.52 [0.34–0.79]*	0.65 [0.45–0.93]*	0.73 [0.50–1.07]
Heroin/Cocaine Use						
Never	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
Past user	1.10 [0.79–1.52]	0.87 [0.60–1.26]	0.60 [0.43–0.83]*	0.58 [0.40–0.83]*	0.94 [0.73–1.21]	0.76 [0.56–1.02]
Current user	0.41 [0.27–0.61]*	0.35 [0.23–0.55]*	0.22 [0.15–0.34]*	0.30 [0.19–0.47]*	0.75 [0.51–1.11]	0.76 [0.50–1.18]
Depressive Symptoms	0.95 [0.93–0.98]*	0.97 [[0.94–1.01]	0.92 [0.89–0.94]*	0.93 [0.90–0.96]*	0.96 [0.93–0.98]*	0.96 [0.93–0.99]*

* p < 0.05

** models adjusted for age, race, sex, time enrolled in care, alcohol use, heroin/cocaine use and depressive symptoms

*** 5 interviews without report of adherence and HIV-RNA was available (resulting in 5 additional interviews and one additional individual)