Published in final edited form as:

AIDS Behav. 2017 July ; 21(7): 2005–2013. doi:10.1007/s10461-017-1782-x.

Cannabis Use, Medication Management and Adherence among Persons Living with HIV

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Abstract

Cannabis is used to relieve nausea, trigger weight gain, and reduce pain among adults living with HIV; however, the relationship between its use and medication adherence and management is unclear. Participants (N = 107) were from an ongoing cohort study of community-dwelling HIV+ adults, stratified by cannabis (CB) use: HIV+/CB+ (n = 41) and HIV+/CB− (n = 66). CB+ participants either tested positive in a urine toxicology screen for THC or had a self-reported history of regular and recent use. HIV-status was provided by physician results and/or biomarker assessment. Adherence was measured via the Morisky scale and medication management was assessed via the Medication Management Test-Revised. After adjusting for gender, we found no association between cannabis use group and adherence nor medication management. The amount of cannabis used was also not associated with measures of adherence and management. Preliminary findings suggest that cannabis use may not adversely influence medication adherence/management among adults living with HIV.

Keywords

cannabis; adherence; medication management; HIV

INTRODUCTION

The prevalence of cannabis use remains high among the general population (1) and it is the most commonly used drug among adults living with HIV (2). The recreational and medicinal use of cannabis may be increasing among individuals with HIV due to growing reports of its potential to treat and manage symptoms of HIV/AIDS (3, 4). For example, cannabis may help to relieve nausea, trigger weight gain, and reduce pain and anxiety (5–8). However, the medical benefits of cannabis (and/or its active constituents), as well as its harmful effects, continue to be ardently debated (9–12). Regardless, at this time, over half of the United

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COMPLIANCE WITH ETHICAL STANDARDS

No author has a conflict of interest to report. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

States (28 states) has legalized medicinal cannabis to treat HIV/AIDS-related wasting and other approved diseases (13). States that have legalized medicinal cannabis report higher rates of use (13), suggesting that cannabis use among adults living with HIV is not likely to decrease. Thus, it is critical to understand how use of cannabis may influence individuals living with HIV.

Adherence to antiretroviral therapy (HIV medication) is required for therapeutic success among adults living with HIV (14). Substance use has been extensively documented as a key predictor of non-adherence (15–19); however, there is a lack of consensus on the topic of cannabis use, specifically, and adherence among adults living with HIV (20, 21). Corless et al. (22) reported poor adherence qualities among cannabis users such as more concerns or worries about their medications, more total reasons for missed medications, and more problems taking their pills than those who did not use cannabis. Yet, de Jong et al. (2005) (23) reported a trend toward higher adherence among HIV patients with moderate to severe nausea who use cannabis. There are also studies that report no significant association between cannabis use and medication adherence (21, 24). In addition to the unclear findings in the current literature, studies only report on medication adherence and not medication management, which is important to evaluate given its documented decline among HIV patients (25).

Neurocognitive functioning is known to be affected by HIV (26–28) and has been associated with medication adherence and management (25, 29–31). There have been reports of negative correlations between medication management and attention/working memory, executive function, learning, and memory (25). Therefore, there are concerns that the use of cannabis may have an increased negative impact on medication management and adherence. Independent of HIV status, cannabis has been associated with impaired cognition, memory, and other adverse neuropsychological outcomes (12, 32–37) that are especially important among adults living HIV.

Despite these independent effects, minimal published studies have examined the relationship between cannabis use and medication adherence and management. Therefore, the purpose of the current study was to examine whether or not cannabis use makes an impact on medication management and adherence among adults living with HIV.

METHODS

Study Population

Adults (18–60 years) were recruited via word-of-mouth and through flyers distributed throughout the Southern Florida area in strategic locations such as local stores, “smoke shops”, infectious disease clinics, and community agencies as part of a larger study aimed to examine the impact of cannabis use on neuropsychological functioning of individuals living with HIV/AIDS. The current study examined HIV+ participants grouped by their history of cannabis use [HIV+/CB+ (n = 41); HIV+/CB− (n = 66)].

At screening, participants were excluded if any of the following were present: less than 8 years of education; significant difficulties reading or comprehending English; history of

learning disabilities or other developmental disorders; history of AIDS defining Central Nervous System (CNS) illness or other neurological disorders; severe psychiatric disorder (e.g., schizophrenia, schizoaffective disorder); positive for hepatitis C; open head injury or closed head injury with loss of consciousness for greater than 30 minutes; current treatment with benzodiazepines, opiates, 1st generation or typical neuroleptics, dronabinol (or any other synthetic cannabinoid), amphetamines, or barbiturates; self-report of use within the last 30 days and/or positive urine toxicology screening or for amphetamine, barbiturate, benzodiazepine, buprenorphine, cocaine, ecstasy, methadone, methamphetamine, opiates, oxycodone, phencyclidine, and propoxyphene using DrugCheck ® (Express Diagnostics, Int'l., Inc., Blue Earth, MN) or Rapid Tox Cup II ™ (American Bio Medica Corporation, Kinderhook, NY). This extensive set of exclusion criteria were to rule out potential confounds that may impact neurocognitive functioning. Once the participant was determined eligible, those who were considered cannabis users were asked not to engage in cannabis use for 24 hours prior to the study visit. Signs of acute intoxication, or self-report of use within the past 24 hours of the study visit were considered grounds for rescheduling. After enrollment, two participants were excluded from the analyses for endorsing past 30-day use of cocaine (n = 1) and inhalants (n = 1). One participant was excluded from the analyses for meeting the DSM-V criteria for stimulant abuse within the past year.

Measures

Enrolled participants completed urine toxicology testing, breathalyzer testing, paper/pencil and computerized testing of mood, behavior, mental health, substance use, and neurocognitive performance and functional behaviors that lasted approximately 4 to 6 hours. Demographic characteristics such as age, gender, race/ethnicity, and years of education were collected via self-report. IQ was estimated using the Wechsler Test of Adult Reading (WTAR) Word List (38) which prompted participants to read aloud up to 50 words that have irregular grapheme-to-phoneme translation. The WTAR provides normative data available by age, education, gender and ethnicity. All assessments were led by trained examiners in a private office. The Institutional Review Board approved the study protocol and materials.

HIV Serostatus

Participants stratified to the HIV+ group provided proof of their HIV serostatus from their physician or underwent screening the day of the assessment using the OraQuick ADVANCE® Rapid HIV-1/2 Antibody Test (Orasure Technologies, Inc., Bethlehem, PA). CD4+ lymphocyte counts and HIV plasma viral load were provided by the patient via medical records if they were obtained within one month of assessment; otherwise, blood samples obtained on the day of assessment underwent a CBC and lymphocyte subset panel to quantify absolute CD4+ counts.

Cannabis Use

Cannabis use was preliminarily assessed at screening and was assessed in more detail during the study visit. Specifically, to be included in the CB+ group, participants must have reported: more than one year of regular cannabis use; use of cannabis at least 1 time a week (on average) during the past 12 months; use of cannabis at least 4 or greater times in the prior month; more than or equal to 196 lifetime occasions of cannabis use. Participants in

the CB− group did not meet any of the criteria for CB+ users and reported no cannabis use in the last 6 months. Detailed information on substance use history was collected using the Drug Use History Questionnaire, an interviewer-administered semi-structured interview querying for various substance use characteristics (e.g., amount, frequency, age of first use, route of administration) for various substances (e.g. cannabis, alcohol, tobacco, etc.) across a participant's lifespan (39– 41). The Substance Use Disorders Module of the Structured Clinical Interview for DSM-IV Disorders was administered to assess substance abuse and dependence (42). In addition to self-report measures, all CB+ participants underwent a urine toxicology testing to quantify levels of THC metabolites (9-carboxy-THC) using liquid chromatography mass spectrometry with a 1ng/mL level of detection.

Medication Adherence

Medication adherence was assessed with selected questions from the Modified-Adult AIDS Clinical Trial Group (M-ACTG) questionnaire (43). This 21-question self-report questionnaire asks about the participants' HIV medication regimen and how often they miss doses. Medication adherence was also examined using the 4-item Morisky Scale (44). Participants were asked if they forgot to take their medication, were careless at times about taking medication, stopped taking medication sometimes when they felt better, and whether or not they stopped taking medication if they felt worse after taking it. Participants were considered adherent if the Morisky score was less than or equal to 2.

Medication Management

Medication management was examined using the revised version of the Medication Management Test (MMT-R) (27). This task mirrors the medication management required of HIV+ patients by requesting participants to accurately dispense daily and weekly dosages of medication as well as answer important questions regarding three mock medications.

Specifically, the MMT-R is a measure of one's ability to accurately dispense medications according to a fictitious prescription regimen and answer questions about mock medications. Scores are based on the total percentage of prescriptions that participants place in the medication organizer correctly. Consistent with prior research (25, 27) an ideal score is greater than 60%.

Mental Health

Depression and anxiety were assessed using the Beck Depression Inventory — 2nd Edition (BDI-II) (45) and the Beck Anxiety Inventory (BAI) (46), respectively. The BDI-II and BAI are both 21-item multiple choice self-report questionnaires used to assess amount and severity of symptoms associated with clinical depression and anxiety disorders.

Statistical Analyses

A cross-sectional analysis was conducted using Statistical Analytic Software (SAS) Version 9.3 (SAS Institute, Inc., Cary, NC, USA). Prior to analysis, data were examined for missing values and outliers. Frequencies were used to compare descriptive characteristics as well as prevalence estimates of medication adherence and ideal medication management. T-tests were used to compare means between CB+ and CB− groups. Two logistic regression models

were conducted to assess the binary variable for adherence (Morisky score ≤ 2 = adherent) and ideal medication management (MMT-R of 60% or higher = ideal). Potential covariates were identified using Chi-Squared tests ($p < 0.20$). Only gender fit the criteria to be considered a covariate and was included in all models. Two linear regression models were conducted to examine potential relationships between the amount of cannabis used and the continuous adherence and medication management scores. Two-tailed P values that were ≤ 0.05 were considered statistically significant.

RESULTS

Sample Characteristics

Table I describes demographic and clinical characteristics of the overall sample (N = 107) stratified by cannabis use group (CB+ n = 41; CB− n = 66). The mean age of participants was 37 years (SD: 10.5) and there were more males in the CB+ group than CB− group (82.9% vs 54.5%, respectively; $p = 0.003$). The majority of the sample consisted of race/ethnic minorities, which remained true for both the CB+ and CB− groups. There were no significant differences in years of education, Full Scale IQ, BDI-II, or BAI values between CB+ and CB− groups.

Substance Use

Table II describes current and lifetime substance use behaviors among the sample by cannabis use group.

Cannabis Use—The mean age of cannabis initiation among the CB+ group was 17.2 (SD: 6.4) years. As expected, there were significant differences in the days since last cannabis use, amount of cannabis used in lifetime, and amount of cannabis used in the past year between CB+ and CB− groups. On average, cannabis users used 31.7 grams (SD: 48.0) of cannabis in the past 30 days. Ten percent (9.8%) of cannabis users met DSM-IV criteria for current cannabis abuse or dependence. Twenty percent (19.5%) met criteria for lifetime cannabis abuse and 12.2% met criteria for lifetime cannabis dependence. About half of the CB− group (47.4%) tried cannabis once in their lifetime; however, none were current users or met the DSM-IV criteria for current cannabis abuse or dependence. Only one participant in the CB− group reported lifetime history of cannabis dependence, but it was sufficiently remote and did not warrant exclusion.

Alcohol Use—There were no significant differences in the reported amount of times alcohol was used in the past 30 days between CB+ and CB− groups. None of the participants reported current alcohol dependence. One participant in the CB+ group reported alcohol abuse within the past year; none was reported among the CB− group.

Other Substance Use—There was a trend toward significance in the differences in the amount of times nicotine was used in the past 30 days between CB+ and CB− groups ($p = 0.06$). There were no significant differences in lifetime substance use dependence or abuse of sedatives, stimulants, opioids, cocaine, or hallucinogens between the CB+ and CB− groups.

HIV Status

Overall, there were no significant differences in any HIV biomarkers between the CB+ and CB− groups. Specifically, the median CD4 count among CB+ was 628 cells/uL (Interquartile Range [IQR]: 380–723) and 607.7 cells/uL (95% CI: 531.8 – 683.6) among the CB− group (p = 0.57). Furthermore, there were no significant differences in HIV plasma viral load (Log10) between the CB+ (0.0 copies/mL; IQR: 0.0–1.6) and CB− (0.0 copies/mL; IQR: 0.0–1.9) groups (p = 0.60). The majority of participants reported the use of the "All-in-one Combination Tablet". Specifically, 61.0% of the CB+ group reported the use of the "All-in-one Combination Tablet" compared to 47.0% of the CB− group (p = 0.16). There were no differences in the prevalence of other HIV related medication (e.g. Protease Inhibitors, Nucleoside Reverse Transcriptase Inhibitors [NRTIs], Non-Nucleoside Reverse Transcriptase Inhibitors [NNRTIs], Fusion Inhibitors, or Integrase Inhibitors) between CB+ and CB− groups.

Medication Adherence and Management

The majority of both CB+ and CB− groups were adherent to their medication regimen based on Morisky scores. Specifically, 87.8% of cannabis users and 80.3% of non-cannabis users were adherent (p = 0.31). The mean Morisky total score among the CB+ group was 0.74 (SD: 0.76) which was not significantly different from the CB− group score of 0.65 (SD: 0.96; p = 0.62). There were no significant differences in the MMT-R total score between the CB+ and CB− groups (11.8 vs 11.2, respectively; p = 0.39). The majority of cannabis users (70.7%) had ideal medication management compared to 56.1% of non-cannabis users (p = 0.13).

Table III details potential predictors of medication adherence and ideal medication management. Race/ethnicity, age, IQ, depression, anxiety, and alcohol use were not significantly different between CB+ and CB− groups; therefore, they were not included in regression models as covariates. After adjustments for gender, cannabis use did not significantly increase or decrease the odds of meeting neither medication adherence nor ideal medication management. Self-reported lifetime, past year, and past 30-day amount of cannabis used did not significantly impact neither medication adherence nor medication management either (data not shown). Similarly, no relationships were observed between 9-carboxy-THC in urine and medication adherence or management. A post-hoc analysis was conducted to examine potential relationships between cannabis use, medication management, and adherence within the CB+ group. Frequency of lifetime, past year, and past 30-day cannabis use did not significant impact medication management nor adherence with the CB+ group. There was a significant correlation between 9-carboxy-THC in urine and medication management (r = −0.33, p = 0.049). After adjusting for gender in the logistic regression model, no significant associations were found (AOR: 0.998, 95% CI: 0.995–1.000).

DISCUSSION

The current study examined the relationship between cannabis use and medication adherence and management among adults living with HIV. There were no significant

differences in medication adherence nor medication management between cannabis users and non-users. Furthermore, the amount of self-reported cannabis used and amount of THC metabolites (9-carboxy-THC) in urine did not have a significant impact on medication adherence nor medication management among adults living with HIV. Findings suggest that cannabis use among HIV+ individuals does not appear to have a significant impact on medication adherence and management in our sample. This is an important consideration given the recent, rapid changes in laws throughout the United States facilitating access to cannabis among individuals with HIV.

Our findings are generally consistent with the limited literature that examines adherence among cannabis users living with HIV. A study of high-intensity cannabis users in Canada (24) found no association between high-intensity cannabis use and adherence to HIV medication. However, the study sample included participants who endorsed other drug use, such as cocaine and heroin. The current study excluded for significant heavy use of other drugs and did not include such participants, especially given the extensive literature showing low adherence among cocaine and heroin users (18, 20, 47). Similarly, a study was conducted to examine cannabis use and adherence among HIV patients with moderate to severe nausea (23). Results from the study indicated that there were no associations between cannabis use and adherence. In addition, similar to our findings, there was not a significant dose-response relationship with regard to amount of cannabis consumed and adherence.

Although our findings are generally consistent with the literature, there are studies that report poor adherence outcomes among cannabis users. For example, a sub-analysis of a longitudinal multisite randomized control clinical trial (22) found that cannabis users were significantly less likely to be adherent based on three of four adherence measures. Specifically, cannabis users had more concerns or worries about their medications, had more total reasons for missed medications, and reported more problems taking their pills. There was no difference between cannabis users and non-cannabis users with regard to forgetting to take medication. There were also no differences between cannabis users and non-cannabis users with regard to the individual components of the Morisky scale (careless about taking medication, forget to take medication, stop taking medication when participants felt better, and stop taking medication because it made participants feel worse). Our results were similar to Corless et al. 2009 with regard to the “forgetfulness” question, indicating that cannabis use did not increase the likelihood of forgetting to take HIV medication.

One of the strengths of the current study is the inclusion of medication management parallel to medication adherence. Most studies only report medication adherence, but medication management capacity, as assessed in the laboratory with a performance-based measure, is important to evaluate given its documented decline among HIV patients (25). At the time of this study, there were no published peer-reviewed studies that were designed to specifically examine the relationship between cannabis use and medication management among adult HIV patients. Findings from our study contribute preliminary evidence indicating no significant association between cannabis use and HIV medication management. Further studies should be conducted to examine this lack of association more closely. Other strengths of the current study include the multiple methods in the measurement of cannabis

use (self-report and urine toxicology) and structured interviews to assess medication adherence and management using validated instruments by trained research staff.

Despite the strengths of our study, there are also limitations. Measures of adherence and medication management are self-report and a study that monitors actual medication use (e.g., with the use of MEMS caps) would further extend our findings. To offset these concerns, it is important to consider that despite the self-report nature of the medication adherence instruments, the measures are validated and include real-life examples using "real" medication. Furthermore, a laboratory measure of medication management was also included in our study with similar results. Despite controlling for potential covariates, there may have been a possibility of confounding due to unknown factors which may have influenced the association between cannabis use and medication adherence and management. Another limitation may have been due to the sample size. A post-hoc power analysis was conducted to see what sample size may be needed to detect an effect. A total of 200 participants would be needed to have a power of 80%. Due to the sample size and insufficient power, there may have been a small effect that was unable to be detected. In this sample, use of cannabis did not show increased risk for poor medication management and adherence; however, it is not possible to generalize to individuals with much higher use of cannabis, those specifically with cannabis dependence (since there were few in the sample), or to cannabis users that are currently using other substances. Furthermore, the current study population was restricted, thus generalization to populations excluded from the study, for example, those with Hepatitis C, is a challenge. Finally, this study consists of cross-sectional analyses that cannot infer causation. Future longitudinal studies should be conducted to examine these relationships more closely.

CONCLUSION

Findings suggest that cannabis use among adults living with HIV does not appear to have a significant impact on medication adherence and management. Future studies should consider differences in medication adherence and management among those who use medicinal cannabis and those who engage in recreational use, as well as other factors that may influence the relationship between cannabis use and medication adherence/management.

Acknowledgments

This work was approved by Florida International University's Institutional Review Board and was supported by grants R01 DA031176 & R01 DA033156 (PI: Gonzalez) from the National Institute on Drug Abuse. All participants provided informed consent.

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Table I

Clinical Characteristics of HIV+ Adults with and without Cannabis Use

	Overall Sample N = 107	CB+/HIV+ n = 41	CB−/HIV+ n = 66	P-value
Age, mean (SD)	37.0 (10.5)	36.4 (9.9)	37.4 (10.9)	0.62
Gender, n(%)*				0.003
Male	70 (65.4)	34 (82.9)	36 (54.5)	
Female	37 (34.6)	7 (17.1)	30 (45.5)	
Race/Ethnicity, n (%)				0.90
Non-Hispanic White	13 (12.1)	6 (14.6)	7 (10.6)	
Non-Hispanic Black	61 (57.0)	22 (53.7)	39 (59.1)	
Hispanic	31 (29.0)	12 (29.3)	19 (28.8)	
Other	2 (1.9)	1 (2.4)	1 (1.5)	
Years of Education, mean (SD)	13.7 (2.4)	13.9 (2.2)	13.6 (2.5)	0.44
FSIQ, mean (SD)	96.8 (11.9)	98.5 (12.4)	95.7 (11.5)	0.24
	CB+ n = 41	**CB− n = 66**		**P-Value**
WCST, T-score mean (SD)	40.9 (10.2)	40.9 (7.7)	40.9 (11.5)	0.98
BAI, mean (SD)	4.7 (6.1)	5.5 (6.7)	4.3 (5.7)	0.32
BDI, mean (SD)	6.3 (6.9)	6.8 (6.5)	6.0 (7.2)	0.54

FSIQ: Full Scale IQ

BAI: Beck Anxiety Inventory

BDI: Beck Depression Inventory

Table II

Substance Use among HIV+ Adults with and without Cannabis Use

Cannabis Use[†]			
Age of cannabis initiation	17.2 (6.4)	20.6 (5.4)	0.01
Days since last cannabis use	4.5 (2.1)	4,456 (4525)	<0.0001
Days used in past 30 days	19.0 (11.6)	0 (0)	<0.0001
Amount[*] used in lifetime	10,278.1 (15,406.1)	42.8 (94.4)	0.01
Amount[*] used in past 12 months	448.6 (680.4)	0.15 (0.30)	0.01
Amount[*] used in past 30 days	31.7 (48.0)	0 (0)	0.01
9-carboxy-THC, ng/mL	314.6 (506.6)	0 (0)	<0.0001
Other Substance Use[†]			
Alcohol, times used in past 30 days	3.9 (6.2)	3.6 (6.7)	0.84
Nicotine, times used in past 30 days	13.1 (14.9)	6.1 (11.3)	0.06
Current DSM-IV Substance Use Disorder[‡]			
Cannabis Abuse	4 (9.8)	0 (0)	0.01
Cannabis Dependence	4 (9.8)	0 (0)	0.01
Alcohol Abuse	1 (2.4)	0 (0)	0.38
Alcohol Dependence	0 (0)	0 (0)	–
Lifetime DSM-IV Substance Use Disorder[‡]			
Cannabis Abuse	8 (19.5)	0 (0)	0.0002
Cannabis Dependence	5 (12.2)	1 (1.5)	0.02
Alcohol Abuse	11 (26.8)	10 (15.2)	0.14
Alcohol Dependence	2 (4.9)	4 (6.1)	0.79
Sedative Abuse	1 (2.4)	0(0)	0.38
Sedative Dependence	2 (4.9)	0 (0)	0.14
Stimulant Abuse	1 (2.4)	1 (1.5)	1.00
Stimulant Dependence	2 (4.9)	1 (1.5)	0.56
Opioid Abuse	0 (0)	0 (0)	–
Opioid Dependence	0 (0)	0 (0)	–
Cocaine Abuse	1 (2.4)	0 (0)	0.38
Cocaine Dependence	3 (7.3)	6 (9.1)	0.75
Hallucinogen Abuse	2 (4.9)	0 (0)	0.14
Hallucinogen Dependence	1 (2.4)	0 (0)	0.38

[†] mean (standard deviation)

[*] amount in grams

[‡] n (%)

Table III

Predictors of Medication Adherence and Management

	Odds Ratio (95 % Confidence Interval)	p-value
Medication Adherence		
Group (Cannabis User, CB+)	0.53 (0.17–1.68)	0.28
Gender	0.79 (0.25–2.40)	0.37
Medication Management		
Group (Cannabis User, CB+)	0.61 (0.26–1.45)	0.26
Gender	1.69 (0.72–3.95)	0.23
	β estimate (Standard Error)	**p-value**
Medication Adherence		
Amount of Cannabis Use	−0.0004 (0.002)	0.88
Gender	−0.04 (0.25)	0.86
Medication Management		
Amount of Cannabis Use	−0.0004 (0.001)	0.69
Gender	−1.69 (0.70)	0.02