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Cannabis use is associated with lower odds of prescription opioid analgesic use among HIV-infected individuals with chronic pain

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Abstract

BACKGROUND—Chronic pain is common in the United States and prescribed opioid analgesics use for non-cancer pain has increased dramatically in the past two decades, possibly accounting for the current opioid addiction epidemic. Co-morbid drug use in those prescribed opioid analgesics is common, but there are few data on polysubstance use patterns.

OBJECTIVE—We explored patterns of use of cigarette, alcohol, and illicit drugs in HIV-infected people with chronic pain who were prescribed opioid analgesics.

METHODS—We conducted a secondary data analysis of screening interviews conducted as part of a parent randomized trial of financial incentives to improve HIV outcomes among drug users. In a convenience sample of people with HIV and chronic pain, we collected self-report data on demographic characteristics; pain; patterns of opioid analgesic use (both prescribed and illicit); cigarette, alcohol, and illicit drug use (including cannabis, heroin, and cocaine) within the past 30 days; and current treatment for drug use and HIV.

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RESULTS—Almost half of the sample of people with HIV and chronic pain reported current prescribed opioid analgesic use (N=372, 47.1%). Illicit drug use was common (N=505, 63.9%), and cannabis was the most commonly used illicit substance (N=311, 39.4%). In multivariate analyses, only cannabis use was significantly associated with lower odds of prescribed opioid analgesic use (adjusted odds ratio=0.57; 95% confidence interval: 0.38-0.87).

CONCLUSIONS/IMPORTANCE—Our data suggest that new medical cannabis legislation might reduce the need for opioid analgesics for pain management, which could help to address adverse events associated with opioid analgesic use.

Keywords

Opioid analgesic; Cannabis; Pain management; HIV

BACKGROUND

Chronic pain is common in the United States and the number of patients with non-cancer pain who are prescribed opioid analgesics has increased dramatically in the past two decades (Atluri, Sudarshan, & Manchikanti, 2014; Modarai et al., 2013; Silberberg et al, 2012). This trend is even more striking in HIV-infected individuals. Approximately 50% of HIV-infected individuals have chronic pain (Breitbart & Dibiase, 2002) and, of these, 30% are prescribed opioid analgesics (Silberberg et al., 2012).

Co-morbid alcohol, cannabis, or other illicit drug use in those prescribed opioid analgesics is common. (Ives et al., 2006) Past history of cigarette, alcohol, and cannabis use are associated with risk of opioid misuse in those prescribed opioid analgesics (Fiellin, Tatrault, Becker, Fiellin, & Desai, 2014). This issue is particularly salient among HIV-infected individuals, who have a high prevalence of illicit drug use (Hartzler et al., 2017). Those who are prescribed opioid analgesics are at risk for misuse, addiction, or overdose; further, those who use opioid analgesics without a prescription or in ways other than how they are prescribed often use other illicit drugs such as cocaine or heroin as well (Ives et al., 2006). There are few data on the concurrent use of cigarettes, alcohol, cannabis, and other illicit drugs in HIV-infected people who are currently prescribed opioid analgesics for pain.

OBJECTIVES

To understand patterns of use of cigarettes, alcohol, and illicit drugs (including cannabis, heroin, and cocaine) in HIV-infected people who are prescribed opioid analgesics, we conducted an exploratory analysis in HIV-infected patients with chronic pain.

METHODS

We conducted a secondary data analysis of screening interviews conducted as part of Project FIRST, a randomized trial of abstinence-reinforcing financial incentives to improve HIV outcomes among HIV-infected drug users that was conducted in the Bronx, New York (deleted-masked authors). The Institutional Review Board at Albert Einstein/Montefiore Medical Center approved this study. All participants provided oral informed consent.

We recruited a convenience sample between June 2012 to June 2015 from Bronx drug treatment programs, Bronx HIV clinics, and newspaper advertisements. We included all participants who completed a screening questionnaire who were: 1) 18 years or older, 2) fluent in English or Spanish, 3) HIV-infected by self-report, and 4) reported a chronic pain condition lasting at least three months measured by an affirmative response to a single question, “Do you currently have a pain condition that causes you pain on most days, and has lasted for 3 months or more?”

We conducted interviews in a private setting at one of Einstein/Montefiore’s clinics or over the telephone. The interview questionnaire consisted of 31 questions, lasted approximately ten minutes, and was based on previously validated questions and scales (Berg, Wilson, & Arnsten, 2012; Knisely, Wunsch, Cropsey, & Campbell, 2008; McLellan et al., 1992; World Health Organization, 2001). Questions examined demographic characteristics, presence of chronic pain, patterns of self-reported opioid analgesic use (both prescribed and illicit opioid analgesics), cigarette, alcohol and drug use (including cannabis, heroin, and cocaine) within the past 30 days, current treatment for drug use and HIV (including utilization of and adherence to antiretroviral therapy [ART]).

Our outcome variable was current use of a prescribed opioid analgesic. We considered patients to be currently prescribed opioid analgesics if they gave an affirmative response to the following two questions: “In the past month have you taken any prescription painkillers that were either prescribed or not prescribed to you? (By painkillers, I mean percocet, oxycontin, codeine, vicodin, dilaudid, morphine and other similar medications)” and “Were any of those prescription painkillers prescribed to you?” Patients giving any other combination of responses were considered to be not currently prescribed opioid analgesics.

Our main exposure variables were participants’ self-reported current use of cigarettes, alcohol, or illicit drugs, including non-prescribed opioid analgesics, cannabis, heroin, and cocaine (within the past 30 days). We collected data on a number of other variables to describe the sample, including self-reported gender, age, race/ethnicity, current methadone maintenance treatment, and use of and adherence to ART. These factors were also considered potential confounders in tests of the association between substance use and prescribed opioid analgesic use.

We conducted bivariate analyses using chi-square and t-tests to examine factors associated with prescribed opioid analgesic use and then multiple logistic regression analyses to examine associations between our main exposure variables and prescribed opioid analgesic use. We included variables in the adjusted models that were associated with prescribed opioid analgesic use at a significance level of $p<0.10$ in bivariate analyses.

We conducted sensitivity analyses to ensure that patterns of substance use and prescribed opioid analgesic use were not solely reflective of our sampling, which included patients in current drug treatment programs. We repeated the above analyses excluding people who were recruited from drug treatment programs (N=95) and those currently receiving methadone maintenance treatment (N=177).

RESULTS

Of the 790 HIV-infected participants screened for the parent study, 459 (58.1%) reported chronic pain. In the group of HIV-infected people with chronic pain, the mean age was 52.0 years, 451 (57.1%) were male, and 721 (91.3%) were Hispanic or non-Hispanic black (see Table 1). Almost half of the sample (N=372, 47.1%) reported current prescribed opioid analgesic use. Illicit drug use was common (N=505, 63.9%), and cannabis was the most commonly used illicit substance (N=311, 39.4%).

As shown in table 1, in bivariate analyses, those with prescribed opioid analgesic use were significantly less likely to report current use of any alcohol or cannabis. People with prescribed opioid analgesic use were significantly older than those without prescribed opioid analgesic use and were significantly more likely to report 100% adherence to ART. Also in table 1, multivariate analyses that included age, ART adherence, alcohol use, cannabis use, and heroin use, found that cannabis use was significantly associated with a lower odds of prescribed opioid analgesic use (adjusted odds ratio=0.57 (95% C.I. 0.38-0.87). This finding remained statistically significant in sensitivity analyses in which people recruited from drug treatment programs or those receiving methadone maintenance treatment were excluded.

DISCUSSION

In a convenience sample of HIV-infected people with chronic pain, nearly half reported prescribed opioid analgesic use and polysubstance use was common. Our analysis of cigarette, alcohol, and illicit drug use patterns found that only cannabis use was independently associated with prescribed opioid analgesic use after adjusting for potential confounders and other substance use. Compared with non-users, those who reported cannabis use were significantly less likely to report prescribed opioid analgesic use.

There are two possible explanations. First, participants who reported cannabis use may have been less likely to be prescribed opioid analgesics by their providers, given concerns supported by data indicating prior illicit cannabis use is associated with greater risk of opioid analgesic misuse (Fiellin et al., 2014). This explanation is weakened by our findings that neither cigarette smoking nor alcohol use, both also found in previous research to be associated with misuse of opioid analgesics (Fiellin et al., 2014), were independently associated with prescribed opioid analgesic use. However, it is possible that providers were not as influenced by their patients' use of legal substances (cigarettes and alcohol) than use of illicit cannabis when deciding whether to prescribe opioid analgesics. We note that all cannabis use at the time of our study was illicit, as our data were collected prior to New York State's implementation of medical cannabis legislation (January of 2016).

A second possible explanation is individuals using cannabis may be less likely to seek prescribed opioid analgesics for pain management than those not using cannabis because cannabis helps them to control their pain. People may prefer cannabis over opioid analgesics for managing their pain, as cannabis may be perceived as safer than opioids or having a more favorable side effect profile (Zaller, Topletz, Frater, Yates & Lally, 2015). Indeed, there is some evidence that appropriate use of medical cannabis might reduce the negative

consequences of addiction that are known to be associated with opioid analgesic misuse (Lucas, 2012).

This explanation is supported by randomized controlled trials of patients with chronic pain that consistently demonstrate that, compared with placebo, cannabis use leads to greater reduction in pain (Andraea et al., 2015; Whiting et al., 2015). While there remain significant gaps in this research, these findings are promising for a search for alternatives to prescribing opioid analgesic in pain management (National Academy of Sciences, Engineering and Medicine, 2017). The exact mechanisms of cannabis' analgesic properties are not fully understood, but have been initially described. Cannabinoids affect two types of receptors: CB1 (mainly found in the brain and spinal cord) and CB2 (mainly found on cells in the immune system). CB1 analgesic activity appears to be via attenuation of neuronal mechanisms and anti-inflammatory effects of mast cells. CB2 analgesic activity appears to involve inhibiting the release of pro-inflammatory factors in non-neural cells as well as indirect stimulation of opioid receptors (Manzanares, Julian, & Carrascosa, 2006). Cannabinoids also directly inhibit acetylcholine, dopamine, and glutamate release, and indirectly affect gamma-amino butyric acid, N-methyl-D-aspartate, and serotonin receptors. Through all of these mechanisms, cannabinoid receptor activation modulates pain, nausea, spasticity, sleep, motor function, and memory and cognition (Borgelt, Franson, Nussbaum, & Wang, 2013).

These findings that medical cannabis is effective for pain management, and may be a desirable alternative to opioid analgesics is particularly relevant in the content of HIV infection. The potential benefit of medical cannabis in the treatment of patients with HIV has a long history (Werner, 2001) and up to 62% of people with HIV infection report cannabis use (Mimiaga et al., 2013; Okafor et al., 2017; Ompad et al., 2016). Cannabis use could improve HIV outcomes by improving pain and anxiety (both are associated with poor HIV outcomes) or could worsen HIV outcomes, as suggested by pre-clinical studies which show that cannabis negatively impacts immune function (Friedman, Klein, Newton, & Daaka, 1995; Hollister, 1992). Further, similar to other substances of abuse, more severe or frequent use could negatively impact HIV outcomes due to reduced adherence. Studies examining the relationship between cannabis use and HIV viral load have had conflicting results (Abrams et al., 2003; Ghosn et al., 2014; Milloy et al., 2015).

Other data support the idea that cannabis use may influence prescription opioid analgesic use. Recent legislation across the U.S. allows physicians to recommend medical cannabis to treat chronic pain. Two studies have been published that demonstrate that medical cannabis legislation is associated with lower rates of opioid overdose deaths (Bachhuber, Saloner, Cunningham & Barry, 2014) and lower prescribing rates of medications to treat conditions for which medical cannabis may be recommended (e.g., opioid analgesics to treat chronic pain; Bradford & Bradford, 2016).

While our findings provide evidence of an association between cannabis use and reduced opioid analgesic use, other studies indicate that, among people with chronic pain who take opioid analgesics, cannabis may allow for a lower opioid dose. Those who use cannabis are more likely than those who do not to have higher pain severity, receive more opioid

analgesic prescriptions, and take higher opioid analgesic doses (Degenhardt et al, 2015; Hefner, Sofuoglu & Rosenheck, 2015), but patients initiating medical cannabis for chronic pain reduced their opioid analgesic doses substantially (44%–64%) in two studies (Boehnke, Litinas & Clauw, 2016; Haroutounian et al, 2016). Further longitudinal studies are needed to understand the true impacts of cannabis use on patients' opioid analgesic use, including dose, as well as pain and function.

There may be some reason for caution when considering medical cannabis use for pain management in HIV. Several studies have reported potential adverse effects of illicit cannabis use, such as other illicit drug use (Volkow, Baler, Compton, & Weiss, 2014), motor vehicle accidents (Li et al., 2012), and hospitalizations (Patel et al., 2016). However, it is uncertain whether these findings on illicit cannabis use can be extended to medical cannabis use.

This study has several limitations. Our study was cross sectional, prohibiting drawing cause/effect conclusions. Ours was a convenience sample drawn from patient populations in the Bronx, New York. Thus, our findings may reflect local drug use and prescribing patterns. Our data were based on self-report rather than biological markers to confirm the use or abstinence of any substance. Further, substance use data were binary (yes/no) rather than more detailed data that included frequency of use or amount used. Finally, the list of substances included in this analysis is limited, and we lack details on both dose and duration of prescribed opioid analgesics and well as amount and frequency of cannabis and other drug use. Despite these limitations, our finding on cannabis use is provocative.

CONCLUSIONS/IMPORTANCE

In our study of HIV-infected people with chronic pain, prescribed opioid analgesic use and poly-substance use were common. Additionally, cannabis use was associated with lower odds of prescribed opioid analgesic use. Continued efforts to monitor and address prescribed opioid analgesic use with concomitant use of other substances are warranted. Further, as the use of medical cannabis across the U.S. grows, examining how cannabis use is associated with prescribed opioid analgesic use and chronic pain management is important, particularly among HIV-infected individuals who have increased need for pain management and are at risk of substance use and abuse.

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Table 1

Characteristics of HIV-infected patients with chronic pain who report taking prescribed opioid analgesics

	Total	Bivariate analyses		Multivariate analysis[a]
Characteristics	**N=459, n (%)**	**Prescribed opioid analgesics N=216, n (%)**	**Not prescribed opioid analgesics N=243, n (%)**	**Adjusted OR (95% CI)**
Demographic characteristics				
Age (mean years ± SD)	52.0	52.8 (7.9)	51.2 (8.5) *	1.01 (0.98-1.03)
Male	262 (57.1)	128 (59.3)	134 (55.1)	–
Race/ethnicity				
Hispanic	213 (46.4)	102 (47.2)	111 (45.7)	–
Non-Hispanic black	206 (44.9)	100 (46.3)	106 (43.6)	
Non-Hispanic white	19 (4.1)	5 (2.3)	14 (5.8)	
Non-Hispanic other	21 (4.6)	9 (4.2)	12 (4.9)	
Clinical characteristics				
ART utilization	430 (94.0)	203 (94.0)	227 (93.8)	–
100% Adherence to ART[b]	86 (20.0)	51 (25.1)	35 (15.4) *	1.00 (1.00-1.01)
Receiving methadone maintenance treatment	177 (39.5)	85 (40.1)	92 (39.0)	–
Current substance use (within the previous 30 days)				
Cigarettes	344 (75.1)	156 (72.2)	188 (77.7)	–
Alcohol	260 (57.0)	109 (50.7)	151 (62.7) *	0.79 (0.53-1.20)
Marijuana	181 (39.4)	68 (31.5)	113 (46.5) *	0.57 (0.38-0.87)
Illicit opioid analgesics	87 (19.0)	39 (18.1)	48 (19.8)	–
Heroin	76 (16.6)	28 (13.0)	48 (19.8) **	0.68 (0.40-1.16)
Cocaine	148 (32.2)	67 (31.0)	81 (33.3)	–
Any Illicit substance[c]	292 (63.6)	126 (58.3)	166 (68.3) *	–

Missing data: 1 ART utilization, 1 hepatitis C virus infection, 1 cigarette use, 3 alcohol use, 11 methadone maintenance treatment

* $p<0.05$,

** $p<0.10$

[a] N=429 because of including only those participants taking ARVs and missing data

[b] N=430, because of including only those participants taking ARVs

[c]Use of illicit opioid analgesics, heroin, cocaine, or marijuana