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Pain symptoms associated with opioid use among vulnerable persons with HIV: An exploratory study with implications for palliative care and opioid abuse prevention

Amy R. Knowlton¹, Trang Q. Nguyen¹, Allysha C. Robinson¹, Paul T. Harrell², and Mary M. Mitchell¹

¹Johns Hopkins Bloomberg School of Public Health, Department of Health, Behavior and Society, Baltimore, MD

²Moffitt Cancer Center, Tampa, FL

Abstract

Current or former injection drug using (IDU) persons with HIV/AIDS are at high risk for pain, which adversely affects quality of life and may increase risk for illicit drug use or relapse. We explored associations between pain symptoms and substance use among IDU study participants with HIV/AIDS and histories of heroin use. Using generalized estimating equations and controlling for prior substance use, pain in each six month period was associated with use of heroin and prescription opioids, but not use of non-opioid drugs or alcohol. Routine clinical assessment and improved management of pain symptoms may be needed in persons with HIV and a history of injection drug use, particularly those with chronic pain, for whom there is increased risk for heroin use.

Keywords

chronic pain symptoms; heroin; prescription opioids; injection drug use; HIV/AIDS; palliative care

Introduction

Pain symptom assessment and management in vulnerable populations have received little attention in research or clinical care though they have major implications for quality of life and health outcomes. Inadequate pain management may affect drug or alcohol use or relapse, especially among persons with serious chronic illness and a history of drug abuse. Injection drug using persons often use opioids and report high levels of pain, which may in part be explained by their high rates of human immunodeficiency virus (HIV)^{1,2} and other pain-related conditions^{3,4}. African Americans comprise the vast majority of HIV

Correspondence concerning this article should be addressed to: Dr. Amy Knowlton, Johns Hopkins Bloomberg School of Public Health, 624 N Broadway, Room 745, Baltimore, MD 21205; Phone (410) 502-4907; aknowlt1@jhu.edu.

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seropositive, injection drug using persons and experience disparities in pain symptoms and management^{5,6,7}.

Having a history of substance use is considered a risk factor for untreated pain in HIV/AIDS patients⁸. Opiate dependent patients may need higher doses and more frequent doses of pain medication due to their reduced threshold for pain⁸. However, physicians may be reluctant to provide these patients with sufficient pain medication due to their history of drug use, which may prompt these patients to find alternate sources of medication⁸. Understanding associations between pain symptomology and drug and alcohol use among high risk, chronically ill populations is important for informing ways to address the opioid abuse epidemic in the US with attention to the needs of vulnerable patient populations. The present study examined prospective associations between pain symptoms and use of prescription and illicit opioids and other drugs in a high risk population engaged in medical care and treatment.

Disparities in HIV-related comorbidities

Injection drug use (IDU) is one of the most prevalent HIV exposure categories in US northeast cities, contributing to almost half of HIV cases in Baltimore, MD, where heroin is the primary drug of choice^{9,10,11}. African Americans, compared to other racial/ethnic HIV groups, are at considerable risk of pain due to their high rates of IDU- and HIV-related comorbidities, including cancer, neuropathy, Hepatitis C, and diabetes^{12,13}. HIV-related neuropathy affects an estimated half of persons with HIV,^{14,15} with African Americans having higher risk^{13,16,17}. While African Americans, irrespective of HIV status, have the highest incidence of cancer among racial/ethnic groups;^{18,19} the high prevalence of tobacco use among African Americans with HIV, approximately 85% in some studies,^{14,15,16,20} contribute to their exceptionally high rates of cancer^{14,16}.

Pain, quality of life, and substance use

Pain has a major impact on quality of life and is a major focus of palliative care, a newly recognized medical specialty that seeks to reduce suffering and promote quality of life among persons with serious illness at any illness stage²¹. Physicians must seek a balance between life-prolonging treatments that may increase longevity but cause greater pain for the patient with the desire to reduce pain and suffering that is the goal of palliative care⁸.

Unrelieved pain is associated with the use of illicit and prescription drugs, opioids in particular^{22, 23}. Of the more than 22,000 pharmaceutical overdose deaths in 2013, 71% were from prescription painkillers²⁴. Overdose is now the second leading cause of death, and has long been the main cause of death for heroin users²⁵. Research suggests that African Americans have disparities in pain symptoms and management, even among those with access to medical care. Healthcare providers have been found to underestimate pain severity of racial/ethnic minority patients, and to less often prescribe them pain maintenance medication^{12, 26, 27}. Injection drug use is associated with further barriers to health care and opportunities for management of chronic conditions and pain^{18, 22, 23,28,29,30}.

Pain management is especially challenging for persons with complex chronic conditions such as HIV and for persons with a history of long term opioid use. Opioid tolerance and

opioid-induced hyperalgesia, or heightened sensitivity to pain, are common among chronic opioid users and difficult to distinguish. Indeed, hyperalgesia may help to explain the high level of pain symptoms among long time heroin users.

Study objective

The objective of this study was to explore associations between pain and use of various opioids and non-opioid drugs in a high risk sample engaged in health care. We hypothesized that pain symptoms would be associated with use of opioids but not use of other substances. The findings have implications for clinical practice, as well as opioid abuse control and prevention. The study findings also have implications for the introduction of palliative care principles into clinical care of the study population, and can inform drug abuse prevention.

Methods

Sample

The data were from the BEACON study, which examined social environments and HIV medical adherence among the study population in Baltimore, Maryland. Recruitment was through clinic- and street-based advertising. Eligibility criteria included HIV-seropositive adult, former or current illicit injection drug use, and currently taking HIV medication.

Measures

Outcome—All measurements were assessed at three time points (baseline, 6 months, and 12 months). The outcome variables were binary variables that represented use of opioid substances (including heroin and prescription opioids) and non-opioid substances (including marijuana, cocaine/crack, and alcohol), measured at time 2 and time 3, with each study participant contributing up to two observations. Substance use was assessed by computer-assisted personal interview and included self-reported use of heroin, prescription opioids (e.g., Vicodin, Dilaudid, Percocet, Darvocet), cocaine, crack, or marijuana in the previous 6 months; and binge drinking in the previous 30 days³¹. Our study assessed use of substances rather than misuse or abuse with the possibility that the medications were prescribed.

Predictors—The independent variable of interest was pain, measured at the same time points as the outcomes. Pain was measured by the question, “How often have you been bothered by pain in the past six months?” with response options never, sometimes, often and always³². Analyses controlled for the use of the same substance measured at the previous time point (time 1 predicting time 2, time 2 predicting time 3), as well as sex and current age.

Analyses—Logistic regression was implemented, regressing the use of each substance on pain, controlling for age, sex and the substance used at the previous time point. To account for clustering of the outcome due to autocorrelation between substance use measures at two time points for the same person, the generalized estimating equation (GEE) method was used³³.

Results

At baseline, the sample (n=383) mean age was 48 years and 61% was male (Table 1). The vast majority (92%) reported past or current use of heroin, and 77% reported attending an academic hospital-based HIV clinic, the study's main recruitment site (data not shown). Table 1 presents the raw person-level data measured at the three time points. Pain symptoms were reported by the majority of participants at all three time points. Fully 79% reported pain at baseline, including 19% who reported always being bothered by pain in the prior 6 months. The re-compiled data used in the analysis comprised 689 observations, including 660 observations from 330 individuals who contributed two observations each, and 29 observations from 29 individuals who contributed one observation each (Table 2).

Logistic regression results indicated that previous substance use was a strong predictor of use for all five of the substances considered, and was the strongest predictor for four of them, excluding prescription opioids (Table 3). Pain was associated with use of both types of opioids (heroin and prescription opioids), after controlling for previous use, age and sex. Compared to those who reported no pain, those who reported any level of pain had substantially elevated odds of prescription opiate use, with a trend of increasing odds of use with increasing pain symptoms (adjusted odds ratio [AOR] = 3.60, 95% CI=1.77-7.31 if *sometimes*, AOR=4.17, 95% CI=1.71-10.14 if *often*, and AOR=9.14, 95% CI=4.27-19.57 if *always* experiencing pain). With regard to heroin use, all three AORs associated with pain were greater than 1 and had a similar trend of AORs of heroin use increasing with rising pain symptoms. However, only the effect of *always* experiencing pain was statistically significant (AOR=2.27, 95% CI=1.22-4.24).

As hypothesized, pain was not associated with higher odds of cocaine/crack or marijuana use (Table 3). With regard to heroin use, all three AORs associated with pain were greater than 1 and had a similar trend of AORs of heroin use increasing with rising pain symptoms (test of trends, $p<.05$). As hypothesized, pain did not predict higher odds of cocaine/crack or marijuana use (Table 3).

Discussion

Consistent with prior studies, the findings suggest high levels of unrelieved pain and risks of illicit opioid use or prescription opioid diversion among this high risk, seriously chronically ill population, especially those with chronic, pervasive pain. Pain symptoms were associated with the use of opioids, including heroin and prescription opioids, but not other drug use, even after adjusting for prior same-drug use. The results suggest significant and selective prescription drug use and self-medicating behavior among the sample, and the need for concerted efforts to improve clinical assessment and management of pain in HIV seropositive injection drug using persons.

Pain, policies, and racial/ethnic disparities

Improving attention to pain in HIV clinical practices is important for promoting quality of life and addressing racial/ethnic disparities in pain^{12, 26, 27}. The sample was engaged in HIV medical care and treatment, mainly at a hospital-based outpatient clinic, which refers

patients with refractory pain to the hospital's pain clinic. Thus, the results likely represent an underestimation of pain symptoms and substance use in the study population.

Current policy approaches to opioid abuse prevention emphasize restricting access to prescription analgesics of abuse potential, especially among persons with high risk for or a history of drug abuse. Research is needed to explore the extent to which such policies contribute to high levels of chronic pain in populations with co-occurring pain-related serious chronic illnesses and substance use disorders. Chronic pain may affect their increased risk for illicit opioid use and relapse, further perpetuating racial/ethnic disparities in pain and jeopardizing patient functioning and quality of life^{34, 35}.

Complexities of pain management

Clinical management of pain among multimorbid patients with a history of or current substance use disorders is complicated by the complexity of etiologies of pain and inadequate health system resources for comprehensively addressing them³⁶, and by clinicians' concerns in prescribing analgesics that may abet their addiction and bring them under scrutiny of prescription opioid control programs³⁷. Also, with limited time or training, it is difficult for clinicians to distinguish opioid tolerance and opioid-induced hyperalgesia in this population, though the two are important to distinguish given that their treatment is diametrically different³⁴. For these reasons, clinicians may tend to under-prescribe analgesics to persons with substance use disorders or to prescribe analgesics less prone to abuse though less effective³⁸.

Research is particularly needed to develop and test comprehensive, including non-pharmacological treatments for pain that address the biopsychosocial context of pain in the study population and its impact on their functioning and quality of life³⁹. For example, research attention is merited to the role of (potentially) supportive others and patient-provider interactions, given their established role in pain perceptions and management⁴⁰. The social stigmas of the study population likely exacerbate their risk for negative interactions that perpetuate pain perceptions and impede pain management^{41,42}.

Palliative care

Integrating palliative care principles into HIV clinical care at any illness stage⁴³, through concerted assessment and pharmacological and non-pharmacological (e.g., physical and psychosocial) intervention, may help to better address the study population's pain⁴⁴ and its adverse effects on quality of life^{23,45}. With its multidisciplinary orientation and focus on alleviating patient suffering and improving functioning and quality of life, palliative care seeks to holistically address patient health and well-being. Importantly, palliative care principles also emphasize the role of patient-provider and family, or supportive, relationships in patient care and outcomes. Research should investigate effects of multimodal, biopsychosocial pain intervention on HIV patients' illicit opioid and other drug use as well as in alleviating pain perceptions and other palliative care outcomes.

Limitations

Our findings are subject to several limitations. Selection of persons engaged in health care and treatment limits the representativeness of the sample to the study population and thus generalizability of the findings. Measurement limitations include lack of distinction with regard to frequency and severity of pain symptoms over time, lack of adjustment for clinical factors and other potential confounders, and inability to distinguish legal versus illegal sources of prescription opioids.

Conclusions

The present study is one of the first to explore associations between pain symptoms and substance use among injection drug using persons with HIV. Our findings highlight the pervasiveness of pain symptoms in injection drug using, primarily African American persons with serious chronic illness^{34, 46, 47}. The findings suggest that opioid prevention policies should balance public health interests of restricting population opioid abuse with patient interests of managing pain. This is important for ensuring such policies avoid unintentionally promoting drug diversion or relapse among persons at high-risk for relapse, and perpetuating racial/ethnic disparities in pain. Future research should further explore factors contributing to pain in the population, and examine ways to promote assessment and adequate management of pain in clinical care, including through palliative care services.

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Table 1

Description of HIV seropositive former or current injection drug using participants on antiretroviral therapy in person-level analysis (Beacon study, n=383).

	Baseline (n=383)	Six months (n=359)	Twelve months (n=331)
	<i>mean (SD) or n (%)</i>	<i>mean (SD) or n (%)</i>	<i>mean (SD) or n (%)</i>
Age in years	48.15 (6.27)	48.85 (6.22)	49.65 (6.19)
Sex			
male	235 (61.4%)	222 (61.8%)	205 (61.9%)
female	148 (38.6%)	137 (38.2%)	126 (38.1%)
Pain [#]			
never	80 (21.2%)	93 (26.0%)	102 (30.8%)
sometimes	175 (46.4%)	164 (45.8%)	132 (39.9%)
often	51 (13.5%)	42 (11.7%)	41 (12.4%)
always	71 (18.8%)	59 (16.5%)	56 (16.9%)
Substance use			
Opioids			
Heroin [#]	130 (33.9%)	84 (23.4%)	72 (21.8%)
Prescription opioids [#]	103 (26.9%)	58 (16.2%)	59 (17.8%)
Non-opioids			
Marijuana [#]	90 (23.6%)	73 (20.3%)	69 (20.8%)
Cocaine or crack [#]	174 (45.4%)	115 (32.0%)	106 (32.0%)
Drinking at least weekly ^{&}	95 (24.9%)	86 (24.0%)	81 (24.5%)
Binge drinking ^{&}	112 (29.2%)	101 (28.1%)	97 (15.7%)

[#] Prior 6 months

[&] Prior 30 days

Table 2

Description of HIV seropositive former or current injection drug using participants on antiretroviral therapy in observation-level analysis (Beacon study; n=689 observations).

	<i>mean (SD) or n (%)</i>
Age in years	49.25 (6.20)
Sex	
male	427 (62.0%)
female	262 (38.0%)
Pain [#]	
never	195 (28.3%)
sometimes	296 (43.0%)
often	83 (12.0%)
always	115 (16.7%)
Heroin use [#]	
previous time	199 (28.9%)
current time	156 (22.6%)
Prescription opiate use [#]	
previous time	155 (22.5%)
current time	117 (17.0%)
Marijuana use [#]	
previous time	149 (21.7%)
current time	142 (20.6%)
Cocaine/crack use [#]	
previous time	265 (38.5%)
current time	221 (32.1%)
Alcohol use, weekly ^{&}	
previous time	170 (24.7%)
current time	167 (24.2%)
Binge alcohol use ^{&}	
previous time	198 (28.7%)
current time	198 (28.7%)

[#] Prior 6 months

[&] Prior 30 days

GEE logistic regression predicting opioid and non-opioid substance use six months later among HIV seropositive former or current injection drug users on antiretroviral therapy (Beacon study; n=689 observations; adjusted odds ratios [AOR] and 95% confidence intervals [CIs]).

Table 3

	Heroin use AOR (95% CI)	Prescription opiate use AOR (95% CI)	Marijuana use AOR (95% CI)	Cocaine/crack use AOR (95% CI)	Binge drinking AOR (95% CI)
Age (years)	0.96 (0.93,1.00)	0.96 (0.93,1.00)	0.99 (0.95,1.02)	0.99 (0.95,1.02)	1.00 (0.97,1.03)
Sex: female	0.58 (0.36,0.92)	0.60 (0.38,0.95)	0.53 (0.32,0.89)	0.65 (0.44,0.98)	0.91 (0.59,1.41)
Previous use	10.59 (6.97,16.07)	4.60 (2.93,7.21)	16.70 (10.55,26.44)	10.33 (7.05,15.13)	14.39 (9.63,21.50)
Pain:					
never	ref.	ref.	ref.	ref.	ref.
sometimes	1.30 (0.77,2.19)	3.60 (1.77,7.31)	1.28 (0.75,2.19)	1.25 (0.79,1.97)	0.96 (0.61,1.52)
often	1.45 (0.71,2.96)	4.17 (1.71,10.14)	1.42 (0.63,3.20)	1.61 (0.85,3.03)	0.95 (0.46,1.98)
always	2.27 (1.22,4.24)	9.14 (4.27,19.57)	1.30 (0.64,2.65)	0.94 (0.52,1.69)	0.57 (0.29,1.09)

Note: Bold denotes AORs that are statistically significant at $p < 0.05$; alpha = .05.

P-values from Wald tests comparing full models to models with only age, sex and previous use (excluding pain) are: 0.21 for heroin use (based on $X^2_{3df}=4.5$); <0.0001 for prescription opiate use ($X^2_{3df}=29.4$); 0.78 for marijuana use ($X^2_{3df}=1.1$); 0.35 for cocaine/crack use ($X^2_{3df}=3.3$); and 0.32 for binge drinking ($X^2_{3df}=3.5$).