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Non-medical use of non-opioid psychotherapeutic medications in a community-based cohort of HIV-infected indigent adults

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Abstract

Background—Non-opioid psychotherapeutic medications significantly increase the risk of opioid overdose-related deaths. We prospectively followed HIV-infected indigent adults sampled from the community to examine rates of and factors associated with non-medical use of benzodiazepines, muscle relaxants, and prescription stimulants.

Methods—We interviewed participants quarterly for 2 years about alcohol and illicit substance use; depression; use of prescribed opioid analgesics, benzodiazepines and muscle relaxants; opioid analgesic misuse; and non-medical use (i.e., use without a prescription) of benzodiazepines,

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muscle relaxants, and prescription stimulants. Using mixed-effects multivariate logistic regression, we determined factors associated with non-medical use of benzodiazepines, muscle relaxants, and prescription stimulants.

Results—Among the 296 participants at enrollment, 52.0% reported taking opioid analgesics that had been prescribed, 17.9% took benzodiazepines that had been prescribed, and 8.1% took muscle relaxants that had been prescribed. Over the 2-year study interval, 53.4% reported prescription opioid misuse, 25.3% reported non-medical use of benzodiazepines, 11.5% reported non-medical use of muscle relaxants, and 6.1% reported non-medical use of prescription stimulants. In multivariable analysis, opioid analgesic misuse in the past 90 days was associated with non-medical use of benzodiazepines, muscle relaxants, and prescription stimulants during the same time interval. Illicit substance use and depression were not associated with non-medical use of these medications.

Conclusions—Prescription opioid analgesic misuse is associated with non-medical use of other psychotherapeutic medications. Health care providers should monitor for non-medical use of a broad array of psychoactive medications among high-risk populations to minimize harm.

Keywords

Benzodiazepines; Muscle relaxants; Non-medical use; Prescription stimulants

1. Introduction

Prescription drug abuse is the fastest growing drug problem in the United States, with more unintentional overdose deaths attributable to prescription drugs than to heroin and cocaine combined (Centers for Disease Control and Prevention (CDC), 2012). Until recently, prescription drug abuse was more common in rural regions, where inadequate access to health care and pain specialists led to the marked increase in the use of opioid and non-opioid psychotherapeutic medications for the treatment of chronic non-cancer pain (Cole et al., 2010; Keyes et al., 2014). However, recent data show that rates for prescription drug abuse or dependence are higher in both large and small metropolitan counties than in non-metropolitan counties (including less-urbanized and rural counties), suggesting that the prevalence of prescription drug abuse is increasing in urban locales (SAMHSA, 2012).

While research has focused on the misuse of prescription opioid analgesics, few studies have focused on the misuse of non-opioid psychotherapeutic medications, which are present in a significant proportion of prescription opioid overdose deaths (Hall et al., 2008; Jones et al., 2012). Benzodiazepines are the most common non-opioid psychotherapeutic medication involved in opioid overdose deaths (Dunn et al., 2010; Gomes et al. 2011; Jann et al., 2014). The concurrent use of opioid analgesics with benzodiazepines, with or without a prescription, has increased significantly in recent years (Jones et al., 2012), and are responsible for the majority of emergency department visits related to abuse and overdose of psychotherapeutic medications (CDC, 2010). Although muscle relaxants and prescription stimulants are implicated less often in prescription opioid overdose deaths (Hall et al., 2008), they are co-prescribed often with opioids (Jones et al., 2012).

Persons living with HIV/AIDS (PLWHA) are prescribed opioid analgesics at high rates and have co-existing mental health disorders and substance use disorders, which are known risk factors for misuse (Vijayaraghavan et al., 2013). Few studies have examined the prevalence and correlates of non-medical use of non-opioid psychotherapeutic medications among PLWHA. We examined these factors in order to provide insights into developing effective prevention and intervention strategies to prevent misuse and overdose.

In this longitudinal study of a community-sampled cohort of HIV-infected indigent adults, we examined rates of and factors associated with non-medical use of benzodiazepines, muscle relaxants, and prescription stimulants. We hypothesized that the misuse of prescription opioids would be associated with non-medical use of these medications.

2. Methods

2.1. Study participants and sampling

We recruited participants from the Research on Access to Care in the Homeless (REACH) study, a longitudinal cohort of homeless and marginally housed HIV-infected adults in San Francisco who were recruited in three waves (1996-1997, 1999-2000, 2003-2004) using population-based sampling from homeless shelters, free-meal programs, and single-room occupancy hotels (SRO; Robertson et al., 2004). Eligible participants needed to be either homeless or marginally housed (living in an SRO that charged less than $600 per month). Each participant was HIV tested at enrollment; those who tested positive for HIV infection were invited to enroll. Approximately 88% of eligible participants enrolled in the REACH study, and enrollees were followed prospectively every 3 months. For the current study (Pain Study), we recruited all REACH participants who completed a quarterly REACH interview during the study enrollment period between September 2007 and June 2008 (n=337) (Miaskowski et al., 2011). The majority (n=306) of the REACH cohort members provided written informed consent to participate in the Pain Study. The final Pain Study sample included 87.8% (n=296) of active REACH participants. The University of California, San Francisco (UCSF) Institutional Review Board reviewed and approved all study protocols. We obtained a Certificate of Confidentiality from the National Institute on Drug Abuse.

2.2. Study Procedures

We met with participants at the UCSF Clinical and Translational Research Institute's Tenderloin Clinical Research Center (TCRC), a community-based university research site. The study included an enrollment interview and seven follow-up interviews over a two-year interval. Trained research assistants administered structured questionnaires. We reimbursed participants $20 for the enrollment and $5 for each quarterly interview, and $20 for each REACH study quarterly interview.

2.3. Non-medical use of benzodiazepines, muscle relaxants, and prescription stimulants

We defined non-medical use of benzodiazepines (e.g., lorazepam, alprazolam, or diazepam), muscle relaxants (e.g., cyclobenzaprine, carisoprodol, baclofen), and prescription stimulants (e.g., dextroamphetamine, methylphenidate) as use without a prescription from a health care

provider. Using Audio Computer Assisted Self-Interview (ACASI) technology, participants self-reported lifetime and past 90-day occurrences of non-medical use of benzodiazepines, muscle relaxants, and prescription stimulants. To assess lifetime non-medical use of benzodiazepines, we asked participants, “Have you ever in your lifetime used sedating or anti-anxiety medications that you got without a prescription from a health care provider?” We asked a similar question to assess non-medical use during the past 90 days at enrollment and at each quarterly visit. We used similar questions to assess non-medical use of muscle relaxants and prescription stimulants, providing examples of drug names for each medication class.

2.4. Opioid analgesic misuse

Participants self-reported opioid analgesic misuse behaviors using ACASI technology at each interview. For each type of opioid analgesic misuse behavior, participants were asked whether they had ever used an opioid medication to engage in that activity (e.g., “to get high.”). We asked a similar question to assess misuse during the past 90 days at enrollment and at each quarterly visit. We defined opioid analgesic misuse as behaviors that posed imminent risk for overdose or legal peril, or aberrant behaviors for which more than 50% of the participants reported that their motivation for the behavior was to get high (Vijayaraghavan et al., 2013).

2.5. Covariates

At the enrollment interview, we assessed lifetime alcohol abuse or dependence using the Diagnostic Interview Schedule-IV (DIS-IV) instrument for alcohol use disorders (Robins et al., 1981). At each quarterly visit, participants self-reported the number of days they drank in the past 30 days and the average number of drinks consumed on days that they drank. We defined problem drinking as > 7 drinks per week for women and > 14 drinks per week for men (National Institute on Alcohol Abuse and Alcoholism, 2005). Using the DIS-IV instrument (Robins et al., 1981), we assessed lifetime substance abuse or dependence for illicit substances (e.g., cocaine, methamphetamine, heroin/opiates). At each quarterly visit, participants self-reported whether they had used any illicit substances in the past 90 days. We identified those who did as current users of illicit drugs.

We defined medical use of a psychotherapeutic medication as use with a prescription from a health care provider. At each quarterly visit, we assessed medical use of a non-opioid psychotherapeutic medication (e.g., benzodiazepines and muscle relaxants) by asking participants, “During the past 90 days have you used any of these medicines that were prescribed to you by a healthcare provider, for pain or any other medical reason?” For medical use of prescription opioids, we asked participants, “During the past 90 days, have you taken any of these medicines prescribed to you to treat pain?” We did not examine medical use of prescription stimulants.

Participants self-reported information on demographics (age and sex), and race/ethnicity (white, African American, Hispanic or mixed/other). We reported lifetime history of chronic homelessness (homeless for at least one year since the age of 18) at enrollment. We assessed depression at each quarterly visit using the Beck Depression Inventory II (BDI-II), and

categorized participants as having no (BDI-II score ≤13), mild (BDI-II score 14-18), or moderate to severe (BDI-II score ≥19) depression (Beck et al., 1996).

2.6. Statistical Analysis

We described sample characteristics at the enrollment visit for categorical and continuous variables. We reported lifetime and past 90-day rates of non-medical use of non-opioid psychotherapeutic medications and opioid analgesic misuse at the enrollment interview and cumulative rates over the study interval (Vijayaraghavan et al., 2013). Using mixed-effects multivariate logistic regression for repeated binary outcomes, we examined factors associated with non-medical use of benzodiazepines, muscle relaxants, and prescription stimulants in the past 90 days. This analysis is equivalent to using generalized estimating equations for repeated binary outcomes with an exchangeable correlation structure (Hedeker, 2003). We adjusted for those variables that were shown to be associated with poly-substance use or adverse outcomes among high-risk populations (Hertz and Knight, 2006; Khosla et al., 2011; Turk et al., 2008). We adjusted for demographic covariates such as age, sex and race/ethnicity (non-white versus white) using values obtained from the enrollment visit. In addition, we controlled for the following time-varying covariates: problem drinking in the past 30 days, illicit drug use, depression, medical use of opioid analgesics, opioid analgesic misuse, medical use of benzodiazepines, and medical use of muscle relaxants. We assessed all time dependent variables (both predictors and outcomes) as the prior 90 days, except for predictor variable problem drinking, which was assessed in the prior 30 days. As opioid analgesics, benzodiazepines, muscle relaxants, and prescription stimulants are co-prescribed often, we wanted to better characterize whether all psychotherapeutic medication carry a similar risk for non-medical use or if one class of medications was a stronger predictor of non-medical use than others. We tested for multicollinearity by calculating the tolerance and variance inflation factor (VIF) from regression models (Fox et al., 2012). The tolerance values were greater than 0.1 and the VIF values were less than 10, thereby providing no evidence for multicollinearity. We conducted these analyses using Stata, version 11.

3. Results

Among the 296 participants, the mean age was 49.4 years (SD 7.5), 71.9% were male, 38.5% were white, and 41.2% were African American. The majority (81.2%) of the participants reported a lifetime history of chronic homelessness, more than two-thirds (69.8%) met criteria for a diagnosis of lifetime substance abuse or dependence, and more than half (58.5%) met criteria for a diagnosis of lifetime alcohol abuse or dependence. At enrollment, 34.8% reported using an illicit substance in the past 90 days, 7.1% reported problem drinking in the past 30 days, and 27.4% reported moderate to severe depression. At enrollment, 52.0% reported medical use of opioid analgesics, 17.9% reported medical use of benzodiazepines, and 8.1% reported medical use of muscle relaxants.

At the enrollment visit, 28.7% reported a lifetime history of non-medical use of benzodiazepines, 14.9% reported non-medical use of muscle relaxants, and 9.5% reported non-medical use of prescription stimulants. The lifetime rate for prescription opioid analgesic misuse was 54.4%. Over the study interval, benzodiazepines (25.3%) were the

most commonly misused non-opioid psychotherapeutic medication, followed by muscle relaxants (11.5%), and prescription stimulants (6.1%). More than half (53.4%) reported opioid analgesic misuse during the study interval. Of the 72 individuals who reported opioid analgesic misuse in the past 90 days at the enrollment visit, 30 (41.7%) reported non-medical use of benzodiazepines, 16 (22.2%) reported non-medical use of muscle relaxants, and 8 (11.1%) reported non-medical use of prescription stimulants over the study duration.

In an adjusted model, identifying as being white (adjusted odds ratio (AOR) 2.1, 95% CI 1.1-3.6), reporting prescription opioid analgesic misuse in the past 90 days (AOR 3.5, 95% CI 2.1-5.7), and taking prescribed benzodiazepines in the past 90 days (AOR 3.7, 95% CI 1.9-7.3) were associated with non-medical use of benzodiazepines in the same 90-day time frame. Being prescribed an opioid analgesic (AOR 2.6, 95% CI 1.2-5.8), reporting prescription opioid analgesic misuse in the past 90 days (AOR 3.4, 95% CI 1.7-6.8), and taking prescribed muscle relaxants in the past 90 days (AOR 9.9, 95% CI 4.2-23.3) were associated with non-medical use of muscle relaxants in the same 90-day time interval. Prescription opioid analgesic misuse was the only variable associated with non-medical use of prescription stimulants in the adjusted model (AOR 5.9, 95% CI 2.1-16.8). Problem drinking, illicit drug use, and depression were not associated with non-medical use of any of the psychotherapeutic medications.

4. Discussion

In this community-based cohort of HIV-infected indigent adults, participants reported significantly higher rates of non-medical use of psychotropic medications than the general population. In a nationally representative study of Americans aged 12 and over, 1.3% reported use without a prescription or in a way other than intended of non-opioid psychotherapeutic medications in the past month (SAMHSA, 2013). The high rate of non-medical use in our study reflects the study's population, which has high rates of mental health disorders and substance use disorders. Despite these risk factors, participants were prescribed opioid and non-opioid psychotherapeutic medications frequently. Our results raise concern that the concurrent use and non-medical use of these medications may increase risk for overdose from opioid analgesics, as these individuals are also at risk for prescription opioid misuse (Vijayaraghavan et al., 2013).

Benzodiazepines are among the most commonly prescribed psychotherapeutic medications, and are used for the treatment of anxiety and as adjunctive treatment for other psychiatric and neurologic conditions (Jann et al., 2014). Our results show that the medical use of benzodiazepines was significantly associated with non-medical use of the same category of medication during the same time period, raising concerns for unintentional overdose. Patients who are prescribed benzodiazepines may acquire additional doses of these medications non-medically to boost the effects of the prescribed medications.

Further raising concerns, we found that opioid analgesic misuse in the past 90 days was associated with non-medical use of benzodiazepines, prescription stimulants, and muscle relaxants during the same time interval. Benzodiazepines can increase the “strength of the drug effect” of opioids (Jann et al., 2014; Jones et al., 2010), which may motivate

individuals who misuse opioid analgesics to use benzodiazepines non-medically and increase their risk for overdose. The rate of non-medical use of prescription stimulants observed in our study was similar to that observed among other high-risk samples (Benotsch et al., 2013; Kelly and Parsons, 2009); however, it was higher than that among a nationally representative sample (Sweeney et al., 2013). Studies have suggested that certain addictive behaviors, such as the misuse of opioids, benzodiazepines, or prescription stimulants, tend to cluster together (Hojsted et al., 2013; Sweeney et al., 2013). Our results support this finding and demonstrate that persons who misuse one type of psychotherapeutic medication may be at risk for misusing other types of medications.

Factors associated with non-medical use of muscle relaxants differed slightly from those associated with non-medical use of benzodiazepines and prescription stimulants. Taking prescribed opioid analgesics or muscle relaxants was significantly associated with non-medical use of muscle relaxants during the same time interval. Some individuals who are prescribed opioid analgesics may acquire muscle relaxants without a prescription to augment the dose effects of opioids. Those who are prescribed muscle relaxants may also seek additional doses of muscle relaxants non-medically to boost the effects of the prescribed medications.

Our study had several limitations. We relied on self-reports of opioid analgesic misuse and psychotherapeutic medications, which may have underestimated prevalence. However, we tried to minimize underreporting by using ACASI technology, which reduces barriers to reporting sensitive information (Williams et al., 2000). Our definition of non-medical use was restricted to the use of psychotherapeutic medication without a prescription and does not include the use of a medication for the feeling it caused, lowering our estimates of non-medical use. Our repeated measures analysis of factors associated with non-medical use of psychotherapeutic medications could be biased if the underlying assumption that the data are missing at random is violated. However, this is less likely as we have no reason to suspect that the relationship between risk factors and outcomes would change significantly after dropout. The results of our study may not be generalizable to non-HIV-infected individuals.

Our results raise awareness of the potential for non-medical use of psychotherapeutic medications that may heighten the risk of overdose from opioid analgesics. The overall high rates of opioid analgesic misuse and non-medical use of other medications in this cohort underscores a need for health care providers to assess for misuse of a broad array of psychotherapeutic medications.

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Highlights

- We found high rates of non-medical use of non-opioid psychotropic medications.
- Persons who misuse opioids also misuse non-opioid psychotropic medications.
- Clinicians should monitor for the misuse of all types of psychotropic medications.

Table 1

Lifetime and past 90-day rates at enrollment, and cumulative rates over the study interval of non-medical use of benzodiazepines, muscle relaxants, and prescription stimulants, and opioid analgesic misuse (N=296)

	Lifetime rate N (%)	Past 90-day rate N (%)	Cumulative rate [d] N (%)
Non-medical use of benzodiazepines [a]	85 (28.7)	26 (8.8)	75 (25.3)
Non-medical use of muscle relaxants [b]	44 (14.9)	10 (3.4)	34 (11.5)
Non-medical use of prescription stimulants [c]	28 (9.5)	5 (1.7)	18 (6.1)
Opioid analgesic misuse [e]	160 (54.4)	72 (24.3)	158 (53.4)

[a] Non-medical use of benzodiazepines including lorazepam, alprazolam, or diazepam

[b] Non-medical use of muscle relaxants including cyclobenzaprine, carisoprodol, or baclofen

[c] Non-medical use of prescription stimulants including dextroamphetamine or methylphenidate

[d] Cumulative rate over 2 year study interval

[e] Defined as any behavior that increases risk for overdose or legal consequences or behaviors for which more than 50% of the participants reported that the motivation for opioid analgesic misuse was to get high

Table 2

Factors associated with non-medical use of benzodiazepines, muscle relaxants, and prescription stimulants in the past 90 days (N=296)

	Non-medical use of benzodiazepines [f] Adjusted odds ratio 95% CI	Non-medical use of muscle relaxants [f] Adjusted odds ratio 95% CI	Non-medical use of prescription stimulants [f] Adjusted odds ratio 95% CI
Age	1.0 (0.9-1.0)	1.0 (1.0-1.1)	0.9 (0.9-1.0)
Male	0.7 (0.4-1.4)	0.7 (0.3-1.6)	0.8 (0.2-2.7)
Race/ethnicity			
Non-white (ref)	1	1	1
White	2.1 (1.1-3.6) [a]	0.7 (0.3-1.5)	2.8 (0.9-8.9)
Problem drinking in the past 30 days [d]	0.6 (0.2-1.8)	1.3 (0.4-4.5)	0.6 (0.1-5.2)
Illicit drug use in the past 90 days [e]	1.5 (0.9-2.5)	0.7 (0.3-1.4)	1.8 (0.6-5.3)
Depression in the past 90 days			
No depression (BDI score ≤13) (ref)	1	1	1
Mild depression (BDI score 14-18)	0.7 (0.3-1.4)	0.9 (0.3-2.4)	0.8 (0.1-4.1)
Moderate to severe depression (BDI score ≥19)	1.3 (0.7-2.2)	1.3 (0.6-2.8)	1.5 (0.5-4.5)
Medical use of opioid analgesics in the past 90 days	1.1 (0.7-1.9)	2.6 (1.2-5.8) [a]	1.6 (0.6-4.6)
Prescription opioid analgesic misuse in the past 90 days	3.5 (2.1-5.7) [c]	3.4 (1.7-6.8) [b]	5.9 (2.1-16.8) [b]
Medical use of benzodiazepines in the past 90 days	3.7 (1.9-7.3) [c]	1.0 (0.4-2.6)	n/a
Medical use of muscle relaxants in the past 90 days	2.1 (0.8-5.4)	9.9 (4.2-23.3) [c]	n/a

[a] $p < 0.05$

[b] $p<0.005$

[c] $p<0.001$

[d] Problem drinking defined as > 7 drinks for women and > 14 drinks for men in the past 30 days

[e] Illicit use of cocaine, methamphetamines, heroin/opiates in the past 90 days

[f] Non-medical use of benzodiazepines, muscle relaxants, and prescription stimulants in the past 90 days