BRIEF REPORT

The Interaction of Alcohol Use and Cannabis Use Problems in Relation to Opioid Misuse Among Adults with Chronic Pain

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Abstract

Background The opioid epidemic is a significant public health crisis and prescription opioids are often used to manage chronic pain, despite questionable long-term efficacy. Furthermore, co-substance (mis)use is also common among individuals with chronic pain who use opioids. Alcohol has been consistently used to manage chronic pain, partly due to its acute analgesic properties. Cannabis has also recently garnered attention in the context of pain management, though research examining its efficacy for pain has produced mixed results. Nevertheless, there is accumulating evidence that concurrent substance co-use is positively associated with use and misuse of additional substances, particularly among individuals with chronic pain. Thus, the goal of this study was to examine the main and interactive effects of alcohol use problems and cannabis use problems in relation to opioid misuse among adults with chronic pain who use opioids.

Methods The current sample was comprised of 440 adults with chronic pain using prescription opioids. Substance use problems were assessed using the ASSIST, Current Opioid Misuse Measure, and the Severity of Dependence Scale. Moderated regressions using the PROCESS macro were utilized.

Results Results indicated that alcohol use problems and cannabis use problems each uniquely related to opioid dependence severity and opioid misuse. The interaction of alcohol and cannabis use problems was uniquely related to only opioid misuse, whereby alcohol use was most strongly associated to opioid misuse among those with higher levels of cannabis use problems.

Conclusions Collectively, these findings suggest there may be utility in assessing and treating alcohol and cannabis use problems among persons with chronic pain who are using opioids for pain management.

Introduction

Chronic pain, defined as pain persisting for at least 3 months, is a significant public health problem affecting millions of people each year [1]. Opioids are often used to manage this chronic pain, despite more recent work suggesting that prolonged exposure to opioids for chronic pain may, in fact, increase sensitivity to pain over time [2]. There is increased recognition that opioid misuse (opioid use without a prescription, at a dose or frequency higher than prescribed, or for a non-medical purpose, e.g., getting high [3]) is prevalent among this population [4], with prevalence estimates as high as 29% [5]. Given that substance co-use, defined as concurrent use (i.e., use occurring within a given timeframe but not necessarily together), is also common among individuals with chronic pain [6], there is utility in examining how the use of commonly used substances may relate to opioid misuse in this population.

Alcohol is one substance that has been consistently linked to the experience of pain [7], and the presence of alcohol use problems [8] may increase the risk for opioid misuse among persons with chronic pain [9–11]. Relative to the general population, individuals with chronic pain endorse higher rates of excessive alcohol consumption and are more likely to meet criteria for alcohol use disorder [12, 13]. Relations between pain and problematic alcohol use operate in a feedback loop [14]; pain is related to a heightened desire to consume alcohol [15], and excessive alcohol consumption is associated with

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more severe and impairing pain [16, 17]. Further, engaging in problematic alcohol use, coupled with increased pain experience, may be associated with seeking additional ways to manage pain, including prescription opioid medication use and misuse [13, 18].

Cannabis is another common form of substance use among the chronic pain population [19–21], and its use is related to a greater likelihood of other substance use [22]. One study found that cannabis use was related to more opioid-related and alcohol use problems among persons with chronic pain [23]. Other research has found that cannabis use in the context of prescription opioid use for chronic pain is associated with fewer opioid-related problems [24, 25]. Yet, no empirical work exploring cannabis use problems in terms of opioid misuse among individuals with chronic pain.

Research conducted among youth and young adults [26], spinal cord injury [27, 28], and persons in treatment for opioid use disorder [29] have reported significant interrelations between problematic cannabis, alcohol, and various forms of opioid use, such that elevated use and misuse of cannabis, alcohol, and opioids have been concurrently observed. Higher levels of alcohol use problems and cannabis use problems may theoretically exacerbate one another to confer greater risk for opioid misuse among a chronic pain population. A formative next step is to examine the potential interplay of alcohol use problems and cannabis use problems in relation to prescription opioid misuse among persons with chronic pain.

The present investigation sought to test the main and interactive effects of alcohol and cannabis use problems in terms of opioid misuse that attempts to build upon the limitations of past work among persons with chronic pain. It was predicted that higher levels of alcohol use problems and cannabis use problems would each uniquely be associated with opioid misuse outcomes, and that alcohol use problems would be associated with greater degrees of opioid misuse among those with higher levels of cannabis use problems, relative to those with lower levels of cannabis use problems.

Method

Participants

Participants were 440 adults (74.3% female, M_{age} = 38.44 years, SD = 11.11) self-reporting current moderate to severe chronic pain and opioid use, who were recruited via an online survey. Eligible participants were between 18 and 64 years of age and reported persistent (at least 3 months) current moderate to severe chronic pain and current use of opioid pain medication. Participants were excluded if they were younger than 18 years, a non-English speaker (to ensure comprehension of the study

questions), or were unable to provide informed, voluntary, written consent to participate. Nine hundred eighty-eight participants responded to the initial survey advertisement, 705 were eligible to participate based on the inclusion criteria, and 445 participants completed the survey. Of the eligible participants, 55.8% endorsed current alcohol use and 39.1% endorsed current cannabis use.

Most of the sample was White (72.5%), with 10.0% identifying as Hispanic/Latino, 7.3% Black/African American, 3.2% Asian/Pacific Islander, 1.4% Native American/Alaska Native, 3.2% multiracial, and 2.4% other. In terms of education, 40.5% of participants reported completing an associate degree or higher. Over a quarter of the sample (31.1%) reported attaining a high school diploma, 22.7% reported "some college," and the remaining 5.7% reported having not completed high school. The median income bracket fell within the range of $35,999 to $49,999.

Measures

Demographics Questionnaire Demographics information including, gender, race, age, education level, income, and marital status was collected.

Current Opioid Misuse Measure The Current Opioid Misuse Measure (COMM) is a 17-item questionnaire designed to detect opioid misuse among chronic pain patients on opioid therapy [30]. The COMM total score was used as a criterion variable ($\alpha = 0.97$).

Severity of Dependence Scale The Severity of Dependence Scale (SDS) is a 5-item measure of gradations of substance dependence (e.g., heroin, cocaine, amphetamine). The SDS has also been validated for opioid use [31] and responses for the current study are anchored to problems associated specifically with opioid use. The SDS total score was used as a criterion variable in the current study ($\alpha = 0.86$).

Graded Chronic Pain Scale The Graded Chronic Pain Scale (GCPS) is an 8-item measure of self-reported pain intensity and disability [32]. Pain intensity items (3) are rated on an 11-point scale from 0 (no pain) to 10 (pain as bad as could be). The GCPS pain intensity ($\alpha = 0.85$) scale was used as a covariate.

The Alcohol, Smoking, and Substance Involvement Screening Test The Alcohol, Smoking, and Substance Involvement Screening Test (ASSIST) is a 7-item assessment for lifetime and current (i.e., past 3 months) use of common substances (tobacco, alcohol, cannabis, cocaine, stimulants, inhalants, sedatives, hallucinogens, and opioids [33]). Six items assess related problems with each substance. In the current study, only the total scores of the ASSIST alcohol use problems

subscale and ASSIST cannabis use problems subscale were used (α's = 0.89).

Procedure

Participants were recruited nationally through Qualtrics, an online survey management system and a validated and representative methodology used in past substance use research [23, 34]. Adults with a Qualtrics Panels account that endorsed moderate to severe chronic pain and current use of opioid pain medication in a Qualtrics pre-screen were sent a survey advertisement. Respondents were screened for eligibility ("Have you had chronic pain (pain that is present most days or every day) over the past 3 months?": none, very mild, mild, moderate severe; "Are you using opioid pain medication?") and directed to the online anonymous survey. Participants provided informed consent prior to completing the survey, which took approximately 30 min. Participants could opt to receive their payment in varying forms (e.g., cash-based incentives [i.e., gift cards], rewards miles, rewards points, etc.). Although the forms were different, the level of compensation remained consistent across respondents ($4.20). The study protocol was approved by the Institutional Review Board at the University of Houston and was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Analytic Strategy

First, sample descriptive statistics and zero-order correlations among study variables were examined. Second, to test the main and interactive effects of alcohol use problems and cannabis use problems on the criterion variables, two hierarchical regression and moderation analyses were conducted in SPSS version 25 using the PROCESS macro [35]. Specifically, three-step hierarchical regression analyses were conducted for current opioid misuse and severity of opioid dependence. In each model, the first step included the following covariates: age [11], gender [36], income [37], education [37], smoking status [38], other drug use [39], and pain intensity [5]. Alcohol use problems and cannabis use problems were then entered together in the second step. An interaction term between alcohol use problems and cannabis use problems was entered in the third step. All continuous variables were mean centered [40]. Further, simple slope post hoc analyses to probe significant interactions were examined to determine the strength of the relationship between the independent variable and dependent variables at levels of the moderator (1 SD below and above the mean [41]).

Results

Bivariate Correlations

Descriptive statistics and zero-order correlations among study variables are presented in Table 1.

Primary Analyses

For current opioid misuse, the first step accounted for a statistically significant amount of variance ($R^2 = 0.31$, $F(7, 432) = 27.5$, $p < 0.001$) and age, gender, education, smoking status, other drug use, and pain intensity emerged as significant predictors (see Table 2). In step two, statistically significant main effects emerged for alcohol problems ($B = 0.49$, SE = 0.08, $p < 0.001$) and cannabis problems ($B = 0.41$, SE = 0.08, $p < 0.001$), accounting for an addition 15% of the variance. The addition of the interaction term between alcohol use problems and cannabis use problems in step three was also significant and accounted for an additional 1% variance in the full model ($\Delta R^2 = 0.01$, $B = 0.02$, SE = 0.01, $p = 0.002$). Simple slope analyses revealed that alcohol use problems were statistically significantly related to current opioid misuse for individuals with both high ($B = 0.60$, SE = 0.08, $p < 0.001$) and low levels of cannabis use problems ($B = 0.31$, SE = 0.09, $p < 0.001$), but the magnitude of the effect was strongest for those with higher levels of cannabis use problems (see Fig. 1).

In terms of severity of opioid dependence, the first step accounted for a significant amount of variance ($R^2 = 0.21$, $F(7, 432) = 16.8$, $p < 0.001$) and age, gender, education, smoking status, other drug use, and pain intensity emerged as statistically significant predictors (see Table 2). At the second step, statistically significant main effects were evident for alcohol problems ($B = 0.06$, SE = 0.02, $p = 0.001$) and cannabis problems ($B = 0.09$, SE = 0.02, $p < 0.001$). The addition of the interaction term between alcohol use problems and cannabis use problems in the third step was not statistically significant ($\Delta R^2 = 0.002$, $B = 0.002$, SE = 0.001, $p = 0.241$).

Discussion

Results were in line with the hypothesis that although alcohol use problems generally would be related to current opioid misuse, this association was stronger among individuals with higher levels of cannabis use problems. These results were evident over and above relevant covariates, including age, gender, income, education, smoking status, other drug use, and pain intensity. These findings are in line with past research demonstrating significant associations between polysubstance and opioid use [26, 27], and uniquely extend these findings to suggest that co-occurring alcohol and cannabis use *problems* may be

Table 1 Descriptive statistics and bivariate correlations among study variables

	1	2	3	4	5	6	7	8	9	10	11
1. Age[a]	1	− 0.01	− 0.05	− 0.02	− 0.12**	− 0.12*	0.16**	− 0.28**	− 0.19**	− 0.26**	− 0.24**
2. Gender[a]		1	0.05	0.07	0.06	0.05	− 0.08	0.25**	0.20**	0.26**	0.22**
3. Income[a]			1	0.41**	− 0.09	0.10*	− 0.01	0.09	0.06	0.10*	0.004
4. Education[a]				1	− 0.04	0.11*	− 0.03	0.14**	0.13**	0.12*	0.04
5. Smoking status[a]					1	0.21**	0.14**	0.29**	0.23**	0.33**	0.34**
6. Other drug use[a]						1	0.06	0.34**	0.29**	0.41**	0.36**
7. Pain intensity[a]							1	0.16**	0.19**	0.03	0.08
8. Opioid misuse[c]								1	0.71**	0.59**	0.55**
9. Severity of opioid dependence[c]									1	0.43**	0.45**
10. Alcohol problems[b]										1	0.59**
11. Cannabis problems[d]											1
Mean, n	38.44	327	5.46	4.33	264	218	21.90	17.83	4.31	8.81	6.72
Standard deviation (%)	11.11	74.3	2.11	1.54	60.0	49.5	5.43	17.02	3.76	10.80	10.01

N = 440

*p < 0.05

**p < 0.01

[a] Covariate

[b] Predictor

[c] Outcome

[d] Moderator

Age = age in years; gender = % listed as female (coded: 0 = female, 1 = male); income (mean, $25,000–$34,999); education (mean, some college education); smoking status = % listed as cigarette smoker (coded: 0 = non-smoker, 1 = smoker); other drug use = % listed as other drug use (coded: 0 = no other drug use, 1 = other drug use); opioid misuse = Current Opioid Misuse Measure (range 0–68, > 9 opioid problem;) [30]; dependence severity = Severity of Dependence Scale (range 0–15) [31, 42]; pain intensity = graded chronic pain scale, pain intensity subscale (range 0–10) [32]; alcohol problems = ASSIST alcohol subscale (range 0–39; low risk) [33]; cannabis problems = ASSIST cannabis subscale (range 0–39; moderate risk) [33]

associated with elevated opioid misuse among adults with chronic pain. Although these results may be clinically important, it is also critical to recognize that opioids may not be efficacious in managing pain [2], and these individuals may be substituting other substances for pain management.

In contrast to expectation, the alcohol-cannabis interaction term was not statistically significant for the severity of opioid dependence. There are several hypotheses that could help explain these results. First, it is possible that the alcohol use problems, in the context of cannabis use problems, may drive craving for opioids (and thus misuse) but may not drive processes such as substance withdrawal, as captured by the SDS. Additionally, the examination of COMM and SDS item content suggests that the COMM measures aberrant drug use behavior as well as emotional and psychiatric problems [30], whereas the SDS measures symptoms associated with a diagnosis of opioid use disorder [31]. Additionally, examining the range of responses suggests a restricted range of scores, with most of the responses clustering on the lower end. Given that the current sample included opioid users, not exclusively those with opioid use disorder, it is possible that the restricted

variability may have reduced power to detect the interaction. Future work could model and extend these findings among individuals with opioid use disorder.

For both current opioid misuse and severity of opioid dependence, there were significant main effects for alcohol use problems and cannabis use problems. These findings suggest that having problems with alcohol or cannabis may uniquely be associated with greater opioid-related problems. Further, examining bivariate effect sizes of the relations between alcohol use problems, cannabis use problems, and opioid-related problems indicated medium to large effect sizes. Thus, a significant proportion of the variance in opioid-related outcomes may be accounted for by alcohol and cannabis. It is possible that alcohol- and cannabis-related problems may, in part, drive opioid-related problems in the context of opioid use for chronic pain. Future work that employs research methodology that can explicate causal pathways between the studied variables is needed.

This study has several limitations. First, the data were cross-sectional, prohibiting causal and temporal claims to be made about the relations. Future longitudinal modeling and experimental designs may help elucidate the directionality of

Table 2 Main and interactive effect of alcohol problems and cannabis problems in relation to opioid misuse and dependence severity

Opioid Misuse	B	SE	t	p	95% Bootstrapped CI		R^2 Change
Step 1							
Age	−0.39	0.06	−6.19	<0.001	−0.52	−0.27	
Gender	8.73	1.51	5.78	<0.001	5.76	11.70	
Income	0.12	0.36	0.34	0.733	−0.58	0.82	
Education	1.12	0.49	2.31	0.021	0.17	2.08	
Smoking Status	6.22	1.46	4.28	<0.001	3.36	9.08	
Other Drug Use	7.95	1.41	5.62	<0.001	5.17	10.73	
Pain Intensity	0.58	0.13	4.50	<0.001	0.33	0.84	.31
Step 2							
Alcohol Problems	0.49	0.08	6.47	<0.001	0.34	0.64	
Cannabis Problems	0.41	0.08	5.28	<0.001	0.26	0.57	.15
Step 3							
Alcohol x Cannabis Problems	0.02	0.01	3.15	0.002	0.01	0.03	.01
Dependence Severity	B	SE	t	p	95% Bootstrapped CI		R^2 Change
Step 1							
Age	−0.06	0.02	−3.99	<0.001	−0.09	−0.03	
Gender	1.61	0.36	4.52	<0.001	0.91	2.31	
Income	−0.01	0.08	−0.08	0.940	−0.17	0.16	
Education	0.24	0.12	2.10	0.036	0.02	0.47	
Smoking Status	0.95	0.34	2.77	0.006	0.28	1.63	
Other Drug Use	1.57	0.33	4.71	<0.001	0.92	2.23	
Pain Intensity	0.15	0.03	4.78	<0.001	0.09	0.21	.21
Step 2							
Alcohol Problems	0.06	0.02	3.32	0.001	0.03	0.10	
Cannabis Problems	0.09	0.02	4.44	<0.001	0.05	0.13	.09
Step 3							
Alcohol x Cannabis Problems	0.002	0.001	1.17	0.241	−0.001	0.004	.002

Note. N = 440. Age = age in years; Gender: coded 0 = female, 1 = male; Smoking Status: coded: 0 = non-smoker, 1 = smoker; Other Drug Use = % listed as other drug use (Coded: 0 = no other drug use, 1 = other drug use); Opioid Misuse = Current Opioid Misuse Measure (Butler et al., 2007); Dependence Severity = Severity of Dependence Scale (Gossop et al., 1995; Iraurgi Castillo et al., 2010); Alcohol Problems = ASSIST Alcohol Subscale (WHO ASSIST Working Group, 2002); Cannabis Problems = ASSIST Cannabis Subscale (WHO ASSIST Working Group, 2002); Covariates included age, gender, income, education, smoking status, other drug use, and pain intensity

Fig. 1 Interaction of alcohol use problems and cannabis use problems predicting opioid misuse. Note: current opioid misuse, COMM [30] Total Score; alcohol use problems and cannabis use problems, ASSIST [33] Substance Involvement Scores. Displayed values of the moderator are 1 SD above the mean and 0
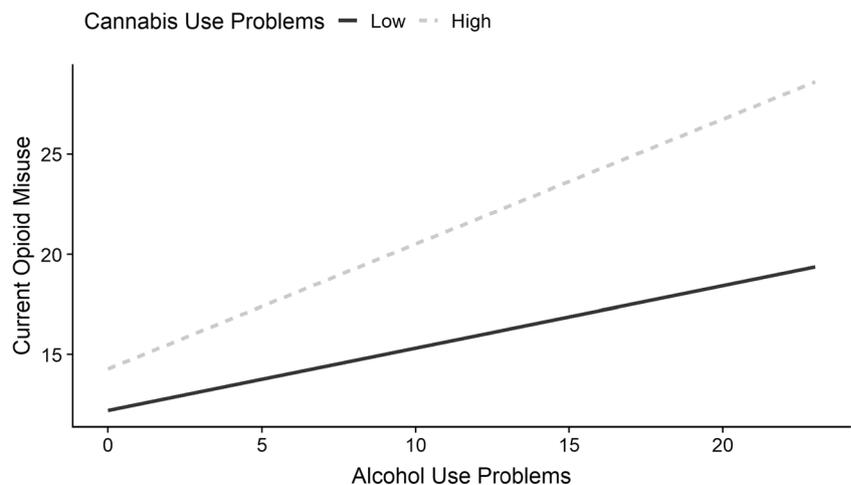
the observed effects. Second, all measures were collected via self-report, and thus, it is possible that results may be due to shared method variance. It is important that researchers attempt to confirm and extend the findings using a multi-method approach. Third, data was collected online, which may have affected the internal validity of the responses. However, it is possible that this method of data collection increased the external validity of the findings due to data collection outside of a controlled laboratory setting [43]. Additionally, while inclusion criteria for the study included a self-reported opioid prescription for chronic pain, it was not verified and therefore it is not possible to determine if the opioids used were, in fact, from a prescription or illicit. Further, given the high proportion of combustible smokers in the current study, it is possible that the additional use of this substance may have confounded the results, and it may be important to explore the impact of combustible cigarette use in future research. Finally, while the current opioid misuse measure is thought to be a measure of overall opioid misuse, examination of item content suggests that the scale measures a combination of aberrant drug-related behavior and emotional problems, with a heavier emphasis on aberrant drug use behavior. As a result, it may be important to replicate these findings using more objective measures of opioid misuse, such as a clinician-administered measure and urine toxicology.

Compliance with Ethical Standards The study protocol was approved by the Institutional Review Board at the University of Houston and was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Conflict of Interest The authors declare that they have no conflict of interest.

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