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Co-occurring prescription opioid use problems and posttraumatic stress disorder symptom severity

Andrea Meier, MS¹, Chantal Lambert-Harris, MA¹, Mark P. McGovern, PhD¹, Haiyi Xie, PhD², Melissa An, BA³, and Bethany McLeman, BA⁴

¹Departments of Psychiatry, Geisel School of Medicine at Dartmouth, Lebanon, New Hampshire, USA

²Departments of Community & Family Medicine, Geisel School of Medicine at Dartmouth, Lebanon, New Hampshire, USA

³Dartmouth College, Hanover, New Hampshire, USA

⁴Dartmouth Psychiatric Research Center, Lebanon, New Hampshire, USA

Abstract

Background—Prescription opioids are the most rapidly growing category of abused substances, and result in significant morbidity, mortality and healthcare costs. Co-occurring with psychiatric disorders, persons with prescription opioid problems have negative treatment outcomes. Data are needed on the prevalence of co-occurring prescription opioid abuse and specific disorders, such as posttraumatic stress disorder (PTSD), to better inform clinical practice. Objective: To determine prevalence rates of current co-occurring prescription opioid use problems and PTSD symptom severity among patients in community addiction treatment settings.

Methods—We abstracted administrative and chart information on 573 new admissions to three addictive treatment agencies during 2011. Systematic data were collected on PTSD symptoms, substance use, and patient demographics.

Results—Prescription opioid use was significantly associated with co-occurring PTSD symptom severity (OR: 1.42, $p < 0.05$). Use of prescription opioids in combination with sedatives (OR: 3.81, $p < 0.01$) or cocaine (OR: 2.24, $p < 0.001$) also were associated with PTSD severity. The odds of having co-occurring PTSD symptoms and prescription opioid use problem were nearly three times greater among females versus males (OR: 2.63, $p < 0.001$). Younger patients (18–34 years old) also were at higher risk (OR: 1.86, $p < 0.01$).

Conclusions—Prescription opioid use problems are a risk factor for co-occurring PTSD symptom severity. Being female or younger increase the likelihood of this co-morbidity. Further

Address correspondence to Andrea Meier, Department of Psychiatry, Geisel School of Medicine, 85 Mechanic Street, Suite B4-1, Lebanon, New Hampshire, 03766 USA. Tel: +1 603 448 0263. ; Email: andrea.l.meier@dartmouth.edu

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research is needed to confirm these findings, particularly using more rigorous diagnostic procedures. These data suggest that patients with prescription opioid use problems should be carefully evaluated for PTSD symptoms.

Keywords

Co-occurring disorders; opioid use disorders; prescription opioid abuse; posttraumatic stress disorder

Introduction

Prescription opioid misuse constitutes the most rapidly growing substance-related problem in the United States (1–8). According to the 2009 National Survey on Drug Use and Health, 5.3 million individuals aged 12 and older (2.1% of the general population) reported current nonmedical use of prescription opioids, such as oxycodone and hydrocodone. Furthermore, an estimated 1.9 million persons have prescription opioid dependence disorder (9). These escalating rates result in negative consequences, including morbidity, mortality and significant healthcare costs (2,3,5,7,10–15). The U.S. Centers for Disease Control determined prescription opioid overdose as the leading cause of accidental death (average of 40 people/day). This number exceeds motor vehicle accidents, and heroin and cocaine overdose combined (16,17). Certain *demographic factors* have been associated with prescription opioid use problems. Individuals of Caucasian race and the 18–25 year old subgroup have been found at increased risk (5,6,18–20). Data on gender as a risk factor is more equivocal (6,12,21). Several studies found similar rates of prescription opioid abuse for women and men (22–25), but a recent study found women at increased risk (26).

Clinical factors, including the use of other substances, have also been associated with increased prescription opioid abuse (2,8,21,23,27,28). Along with other substance use, co-occurring psychiatric conditions, such as depression and anxiety, are correlated with prescription opioid abuse and related to poorer treatment and health outcomes (23,27–31). Treatment approaches for prescription opioid abuse were recently studied, but the moderating effects of psychiatric comorbidities on outcomes were not examined (32–34). Epidemiological and prospective longitudinal data are clearly needed to examine how psychiatric and other addictive disorders interact with prescription opioid abuse.

Posttraumatic stress disorder (PTSD) has been found to co-occur with substance use disorders, and when co-morbid, results in more negative treatment outcomes (35–50). Research has found particularly high comorbidity between PTSD and opioid use disorders, relative to alcohol and other drugs (44,51,52). Women with rape histories have higher rates of prescription drug misuse (20), as do adolescents (12–17 years old) who have witnessed violence (5). Among Veterans, those with a PTSD diagnosis are significantly more likely to engage in high-risk use of prescription opioids, versus those without PTSD (53). A recent civilian study found a prevalence rate of 6.6% for comorbid PTSD and prescription opioid dependence. However, these were non-treatment seeking individuals recruited via advertisements. Therefore generalizability may be limited (54). To date, there are no

published studies on the association between PTSD and prescription opioid use disorders within the civilian treatment seeking population.

The present study examined the prevalence of PTSD symptom severity among individuals with prescription opioid use problems (misuse, abuse or dependence) in three typical community addiction treatment programs.

This study provides data on the following research questions:

1. What is the prevalence of co-occurring PTSD symptoms among those with prescription opioid use problems, relative to other types of substance use problems?
2. Do certain demographic factors, such as gender and age, increase the risk for co-occurring PTSD symptoms and prescription opioid use problems?

Methods

Design

This was a cross-sectional design to evaluate the point prevalence of PTSD symptom severity among persons presenting for services to community addiction treatment agencies. PTSD severity was determined using a standardized self-report measure, the PTSD Checklist civilian version (PCL-C) (55–58). Substance use problem estimates were determined by systematic chart review. Three addiction treatment programs served as sampling sites, with data from each site treated independently in order to test for cross-site variation.

Settings

Admission data were obtained from three large adult community outpatient addiction treatment agencies located in southern, northern, and western cities in a single state (Vermont, USA).

Sample

Patients were seeking treatment for a substance use problem, which may or may not include opioid use disorders. At all three agencies, patients were assessed at intake using the PCL-C (described in the measures section below), and standardized assessments required by the state regulatory authority. There were no exclusion criteria with data from all new admissions gathered. Each program collected uniform data on patient demographics and substance use, including diagnoses and primary, secondary and tertiary substance use. Across all three programs, data from a total of 573 patients were collected, and these comprised the analytic sample.

Measures

PTSD symptom severity—The PTSD Checklist civilian version (PCL-C) is a 17-item, self-report measure with a 5-point scale (1 – *Not at all*, to 5 – *Extremely* bothered by PTSD-related symptoms linked to the most troublesome traumatic event). A total score of 44 or greater constitutes a probable PTSD diagnosis. The PCL psychometrics, including

reliability, validity, sensitivity and specificity estimates have been reported (55–58). The PCL is commonly used and found to have predictive validity for determining PTSD diagnosis (59–70).

Substance use problems—Substance use problem data were extracted from patient charts. Specifically, the Addiction Severity Index (ASI) (71) was used to identify current primary, secondary, and tertiary substance use problems, as well as frequency and duration of use. The ASI has been used to derive and confirm substance use diagnoses in previous research (72). Prescription opioid use problems could include misuse, abuse or dependence.

Demographics—Gender, age, race and ethnicity data were extracted from the agencies' patient records based on their common federal requirements for the U.S. Substance Abuse and Mental Health Services Administration Treatment Episode Data Set (TEDS) reporting.

Procedure

Patients completed the PCL-C at admission. Program staff with access to patient admission records gathered demographic information (gender, age, race and ethnicity), PCL-C scores, and primary, secondary and tertiary substance use problems for all patients admitted during a one-year time frame (2011) and linked these data with the self-report PCLs. Once information was compiled, program staff securely transmitted the de-identified data in aggregate to the research team. Because the archival information collected by program staff was de-identified, participant informed consent was not necessary. The study was conducted in strict accordance with all human subject protections and good clinical practices (e.g. Helsinki Declaration, Belmont Principles, and Nuremberg Code). The Trustees of Dartmouth College Committee for the Protection of Human Subjects (CPHS) approved the collection, analysis and reporting of these data.

Data analysis

Patient demographic characteristics were analyzed initially by frequency analyses. To determine if having a prescription opioid use and/or other substance use problem was associated with PTSD symptom severity, a logistic regression was used. In contrast to frequency analyses with a Chi-square test, a simple logistic regression directly provides the odds ratio and confidence intervals. The dependent variable was PTSD severity (PCL 44) and the predictor variable was prescription opioid use problem. Both the outcome and predictor variables were dichotomous. We employed a multiple logistic regression to examine the predictive relationship between demographic variables (gender and age) and outcomes (PTSD severity; prescription opioid problem; and co-occurring PTSD symptom severity and prescription opioid use problems). Two statistical models were used (simple logistic regression and multiple logistic regression with covariates). There were eight simple logistic regressions and three multiple logistic regression in the analysis plan. Although this is not a large number of statistical tests, there is some risk for Type I error (false positives). Using a correction statistic (e.g. Bonferroni) to reduce this risk is a conservative option (73). However, doing so increases the risk for Type II error (false negatives) (74,75). To balance these risks, we conducted the tests without and with the correction. Significant findings are described in the *Results* section without the corrections, but interpreted in the conclusion

more conservatively (i.e., p value = 0.006). All data were analyzed using the IBM SPSS 21.0 statistical software package (76).

Results

Patient demographics and characteristics

As shown in Table 1, the majority of patients were Caucasian (Not Hispanic or Latino) and between the ages of 26 and 34. More than half of the patients were male; the average PCL score was moderately high for the sample overall. Some 243 of 573 (42.4%) patients were above the symptom severity threshold (PCL ≥ 44), indicating probable PTSD diagnosis. The most frequent type of substance use problem was alcohol, followed by prescription opioids and cannabis. Most patients presented with poly-substance use.

PTSD symptom severity and prescription opioid use problems

A total of 218 (38.0%) patients used prescription opioids along with other substances, while only 27 (4.7%) used prescription opioids exclusively. We collapsed these two variables into a combined “prescription opioids” variable for all subsequent analyses ($n = 245$ [42.8%]). A total of 47% of patients with a prescription opioid use problem had a probable PTSD diagnosis (PCL ≥ 44), while only 38.7% without a prescription opioid use problem likely met criteria for PTSD. A simple logistic regression was used to determine the likelihood for the co-morbidity. As shown in Figure 1, the odds of having severe PTSD symptoms was 1.42 times higher among patients with a prescription opioid use problem (CI: 1.02–1.99; $p < 0.05$). The odds of having severe PTSD symptoms were lower for patients who had a problem with a substance other than prescription opioids (CI: 0.50–0.98, $p < 0.05$).

As shown in Figure 2, the odds of having severe PTSD symptoms was 3.81 times higher for patients with a prescription opioid and sedative use problem (CI: 1.47–9.88, $p < 0.01$). The odds of having PTSD for those with prescription opioid and cocaine use problems were 2.24 times higher (CI: 1.40–3.57, $p = 0.001$). No significant associations between co-occurring PTSD symptom severity and the remaining possible poly-substance use combinations were revealed (prescription opioids + alcohol, prescription opioids + heroin, prescription opioids + cannabis).

Demographic factors and risk for PTSD symptoms and prescription opioid use problems

Demographic variables, gender and age, were evaluated using multiple logistic regressions on PTSD severity or prescription opioid use problems (dichotomous variables). As shown in Table 2, females were at greater risk for prescription opioid use problems relative to males (OR: 1.81; CI: 1.27–2.59, $p < 0.001$). The odds of having severe PTSD symptoms were nearly three times greater for females (OR: 2.63; CI: 1.85–3.73, $p < 0.001$). Nearly a third (30.7%) of the female patient sample had co-occurring PTSD and prescription opioid use problems, while only 13.8% of the male sample had these co-occurring disorders. The odds of having both severe PTSD symptoms and a prescription opioid use problem were 2.64 times higher for females (CI: 1.73–4.02, $p < 0.001$). Age alone did not significantly predict PTSD severity or prescription opioid use problems. Overall model fit was evaluated by Chi-

square tests, and showed that gender and age, collectively, had significant predictive power for the outcomes in all three models.

Patients between the ages of 18–34 were 1.86 times the odds more likely than those 35 and older to have a co-occurring problem (prescription opioid use and severe PTSD symptoms (CI: 1.20–2.89, $p < 0.01$).

Discussion

Summary of findings

This is the first known study to examine the prevalence and risk factors for co-occurring PTSD symptoms and prescription opioid misuse among persons admitted to typical community addiction treatment settings. With regard to the first research question, the data revealed that prescription opioid use problems were associated with an increased risk for PTSD. The type of substances used in addition to prescription opioids, such as sedatives (medications including diazepam, alprazolam, or lorazepam) or cocaine, contributed to even greater risk. In addressing the second research question, two specific demographic factors, age and gender, emerged to compound the likelihood of comorbidity.

We found that for persons with prescription opioid use problems, compared with persons with other substance use problems, there was increased risk for severe PTSD symptoms. This is congruent with a recent study on non-treatment seeking individuals with opioid dependence (54). Results were consistent across the three community addiction treatment programs. Remarkable was the association of prescription opioid use and specific other substance use with PTSD symptom severity. The majority of those with prescription opioid use problems also used other substances. The odds of having severe PTSD symptoms were almost four times higher for persons with prescription opioid and sedative use problems, followed by prescription opioid and cocaine use problems. Prescription opioid use with cannabis, heroin, or alcohol did not demonstrate risk for PTSD.

With regard to demographic risk factors, gender was significant. Similar to recent research, females were more likely than males to have prescription opioid issues (6,12,21,22,24,25,77). Also consistent with previous research, females were more likely than males to have severe PTSD symptoms that meet the severity threshold for diagnosis regardless of type of substance use (36,51,78,79). Examining the co-occurrence of prescription opioid use problems and PTSD, females also had higher prevalence rates than males. There was a moderate association between age (18–34 year range) and the co-occurrence of PTSD symptoms and prescription opioid use problems. Thus, younger adults may be at increased risk.

Limitations

There were four limitations to this study, which can be summarized as follows:

- a. Data gathered upon index admission were correlational and did not provide etiological information or the sequence of the problems. PTSD symptoms may be a risk factor for prescription opioid use problems. These symptoms could increase the

misuse of, and consequential problems related to, prescription opioids (e.g. self-medicating to relieve PTSD symptoms). The alternative sequence is also possible: prescription opioid misuse may lead to an increase in exposure to traumatic events, such as interpersonal violence and motor vehicle accidents, and thereby increase the risk of developing PTSD. We could not test for this association. These limitations are inherent to cross-sectional designs and correlational statistics.

- b. The archival data gathered across the three agencies were uniform and similarly gathered. However the substance use estimates relied on chart diagnoses and ASI summaries, which may have been less valid and scientifically rigorous than structured clinical interviews. The PCL is a commonly used assessment measure, but can be influenced by self-report response biases, and we did not itemize PTSD B, C and D criteria scores (re-experiencing, avoidance, and hyper-arousal). Standardized, clinician-administered measures would add to diagnostic certainty, and strengthen the interpretations of the findings.
- c. Some caution must be exercised in the interpretation of the statistical findings due to Type I error. When applying a Bonferroni correction to these statistics all but one comparison retains statistical significance ($p < 0.006$). This comparison is the odds ratio (OR: 1.42) of prescription opioid problems and PTSD ($p = 0.03$). At increased risk for Type II error by dismissing this finding, a conservative interpretation would identify this relationship as a signal or trend. As with the other limitations to this investigation, a larger sample is needed to confirm these findings.
- d. Finally, although a sample size of 573 patients was achieved, these were primarily Caucasian young adults (26–34 years old) seeking treatment. Although the primary outcomes were consistent across sites, a more diverse and broad sample from community treatment programs across more than one state would add to generalizability.

Clinical implications

These data suggest that community treatment patients with prescription opioid use problems should be carefully evaluated for trauma symptoms and a PTSD diagnosis. Since avoidance is a major feature of PTSD (80), the likelihood of patients under-reporting PTSD symptoms is high. During the early phases of abstinence, without anticipating the emergence of re-experiencing or hyperarousal symptoms, the patient may be at high risk for relapse. The use of opioids for the “self-medicating” purposes of “numbing” or anesthetizing negative affects has been well described (23,81,82). Integrated approaches that address both substance use and PTSD symptoms together and at the same time may be clinically optimal (38,43,83,84). There have been advances in medication assisted treatment options for opioid use disorder, such as methadone and buprenorphine (32–34). The evidence for integrated psychosocial therapies with these medications is mixed (33,85,86). However, integrated psychosocial treatments specifically designed for prescription opioid misuse and psychiatric disorders have not yet been studied.

The association between prescription opioid use problems and PTSD symptom severity may be further compounded by patient abuse of sedatives and/or cocaine. Combinations of substance use problems likely have important clinical implications for complexity and prognosis. Additionally, of the demographic factors examined, gender and age are associated with increased risk for the comorbidity, making it particularly important to screen females and young adults (18–34-year-olds) for the comorbidity.

Future research

Future research, including longitudinal repeated measures designs, broader and potentially more representative samples, and structured diagnostic assessments are needed to confirm the findings. Potential moderators between prescription opioid use problems and PTSD should also be addressed. These may include somatic and other psychiatric concerns that lead to seeking medical care for prescription opioids and/or sedatives. Chronic pain has been highly associated with PTSD (87–90), and those with comorbid chronic pain and PTSD (versus those without PTSD) have shown higher subjective pain ratings, more significant pain-related problems, and high rates of prescription opioid use for pain management, especially among women (25,91,92).

Opioid use disorder treatments have extensively focused on heroin, however persons with prescription opioid use type disorders may require different approaches than those abusing heroin (32–34,51). Given that rates of prescription opioid problems now surpass heroin, further opioid use disorder treatment research with these specific types of substances is warranted. With prevalence rates, risk factors, and moderators more clearly defined, pharmacological and psychosocial interventions targeting prescription opioid use disorders, and the most common psychiatric comorbidities, can be better designed and tested.

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Figure 1.

Odds ratios for posttraumatic stress disorder (PTSD) symptom severity with and without a prescription opioid use problem ($n = 573$). *Note.* * $p < 0.05$.

Figure 2.

Odds ratios for posttraumatic stress disorder (PTSD) symptom severity by prescription opioid use problem in combination with other substances ($n = 573$). *Note:* ** $p < 0.01$; *** $p < 0.001$; categories are not independent; the reference group was patients without a prescription opioid use problem and specific substance combination.

Table 1

Demographic characteristics among patients admitted to addiction treatment.

	New Admissions (<i>n</i> = 573)
Age <i>m</i> (<i>sd</i>)	34.64 (11.72)
	<i>n</i> (%)
18–25	154 (26.9%)
26–34	186 (32.5%)
35–50	164 (28.6%)
51+	69 (12.0%)
Gender (<i>Male</i>)	355 (62.0%)
Race (<i>Caucasian/White</i>)	541 (96.3%)
Ethnicity (<i>Not Hispanic or Latino</i>)	548 (98.9%)
	<i>m</i> (<i>sd</i>)
PCL score	41.10 (17.66)
PTSD symptom severity: Moderate (44–64)	52.60 (5.93)
PTSD symptom severity: Severe (65+)	71.85 (5.53)
	<i>n</i> (%)
Total with PTSD symptom severity above diagnostic threshold (PCL ≥ 44)	243 (42.4%)
Total with moderate PTSD symptom severity	168 (23.0%)
Total with severe PTSD symptom severity	75 (13.1%)
Primary substance use problem single substance only	
Alcohol	118 (20.6%)
Cannabis	11 (1.9%)
Cocaine	3 (0.5%)
Heroin	0 (0.0%)
Prescription opioids	27 (4.7%)
Sedatives	0 (0.0%)
Primary substance use problem in combination with other substances	
Alcohol	353 (61.6%)
Cannabis	200 (34.9%)
Cocaine	159 (27.7%)
Heroin	116 (20.2%)
Prescription opioids	245 (42.8%)
Sedatives	28 (4.9%)

Table 2

Predictive relationship between demographic variables (gender and age) and outcomes using multiple logistic regressions ($n = 573$).

Outcomes	Predictor	Gender + Age		
		OR	CI	χ^2
PTSD symptom severity above diagnostic threshold (yes)	Gender	2.63	1.86–3.73	30.30 ***
	Age	1.00	0.99–1.02	
† Prescription opioid (yes)	Gender	1.81	1.27–2.59	64.45 ***
	Age	0.95	0.93–0.96	
PTSD & Prescription opioid (yes)	Gender	2.64	1.73–4.02	37.29 ***
	Age	0.96	0.94–0.98	

† Prescription Opioid: Prescription opioid use problem alone or other substance use in combination with a prescription opioid use problem;

 $p < 0.001$.