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Chronic pain, craving, and illicit opioid use among patients receiving opioid agonist therapy

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ABSTRACT

Aims: In a sample of patients receiving opioid agonist therapy, we evaluated whether having chronic pain was associated with (a) craving for opioids and (b) illicit opioid use.
Methods: In a cross-sectional study of adults on buprenorphine or methadone maintenance recruited from an urban medical center, we examined any craving for opioids (primary dependent variable) in the past week and recent illicit opioid use (secondary dependent variable). Illicit opioid use was defined as a positive urine drug test (UDT) for opiates and chronic pain was defined as bodily pain that had been present for at least 3 months. Multivariable logistic regression models were fit for each outcome, adjusting for age, sex, and non-white race. Additional models adjusted for depression (PHQ-9) and anxiety (STAI).
Results: The sample included 105 adults on methadone or buprenorphine maintenance. Mean age was 43.8 (SD ±9.4) years; 48% were female and 32% non-white; 19% were on methadone. Chronic pain was present in 68% of the sample, 51% reported craving opioids in the past week, and 16% had a positive UDT. Chronic pain was associated with 3-fold higher odds of reporting craving in the past week (aOR = 3.10; 95% CI: 1.28–7.50, *p*-value = 0.01). The relative odds for having a positive UDT were not statistically significant (aOR = 2.52; 95% CI: 0.64–9.90, p = 0.18).
Conclusion: In this sample of patients treated with opioid agonist therapy, those with chronic pain had higher odds of reporting craving for opioids. Chronic pain with associated opioid craving potentially places this population at risk for relapse.

1. Introduction

In 2014, an estimated 1.9 million people in the United States had an opioid use disorder related to prescription pain relievers, and an estimated 586,000 had an opioid use disorder related to heroin use (SAMHSA, 2015). Chronic pain is common in patients with opioid use disorders who are on opioid agonist therapy (OAT). Studies of patients maintained on methadone or buprenorphine suggest that a third to more than a half report pain that has been present 3 or more months (Barry et al., 2009a, 2013; Jamison et al., 2000; Rosenblum et al., 2003). Chronic pain is highly relevant to substance use outcomes, as it may serve as a barrier to treatment entry, retention or success, and a trigger for relapse. Among HIV-infected substance users, pain has been associated with persistent use of heroin (Tsui et al., 2013). In some studies, patients with chronic pain who received addiction treatment were more likely to relapse to drug use compared to patients without pain (Caldeiro et al., 2008; Larson et al., 2007). However, not all studies have demonstrated

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worse outcomes (Dhingra et al., 2015; Fox et al., 2012; Ilgen et al., 2006).

Drug craving is a subjective phenomenon conceptualized as an individual's desire or urges to use a previously experienced substance (Sayette et al., 2000; Tiffany and Wray, 2012). Opioid craving predicts opioid use among persons with heroin and prescription opioid use disorders (McHugh et al., 2014; Tsui et al., 2014), and treatment with methadone and buprenorphine reduces craving (Fareed et al., 2010). Pain may be associated with increased craving for opioids. Among patients with chronic pain, craving has been associated with aberrant use of prescription opioids (Wasan et al., 2009), and among persons with prior heroin use, increased sensitivity to pain has been associated with opioid craving (Ren et al., 2009). Among patients with treated opioid use disorders, it is unknown whether chronic pain is associated with opioid craving and thereby an increased likelihood of relapse. In addition, the mechanisms whereby pain leads to craving or relapse are relatively unexplored. Prior research suggests that negative affect may be associated with heroin and other drug craving among persons in treatment for opioid use disorders (Epstein et al., 2009; Huhn et al., 2016), and in methadone maintenance treated samples, persons with chronic severe pain have been observed to have more symptoms of depression and anxiety (Barry et al., 2009a).

The study aim is to assess whether having chronic pain was associated with (a) opioid craving and (b) illicit opioid use in a sample of adults who were treated with buprenorphine or methadone for their opioid use disorders. In addition, we explored the roles of anxiety and depression in these relationships to assess whether they might be potential confounders or mediators.

2. Materials and methods

2.1. Objective and study design

This is secondary analysis of a cross-sectional study of adults on methadone or buprenorphine for treatment of opioid use disorders in the VIP (Viral Infections and Pain) study. The parent study explored the contributions of hepatitis C virus (HCV) infection to pain and pain hypersensitivity among persons with treated opioid use disorders on buprenorphine or methadone with and without HCV (Tsui et al., 2015). The current study included all participants whose data on their chronic pain status was available; one subject whose data was missing was excluded. We hypothesized that patients with chronic pain would be more likely to report craving opioids and to have recently used illicit opioids, as evidenced by a positive urine drug test, than those without chronic pain.

2.2. Participants

Study participants were recruited from January 2012 through December 2013 from the Boston Medical Center (BMC). Flyers advertising the study as open to persons who were treated with methadone or buprenorphine for addiction were distributed, and providers were asked to refer interested patients to the study coordinator for screening. Potential subjects were screened over the phone for eligibility and were then invited for a study visit, which included further screening and, if eligible, the study assessment and procedures.

Eligibility criteria included the following: between 18 and 65 years of age, English speaking, receiving primary care at BMC, on methadone or buprenorphine for treatment of an opioid use disorder for at least 4 weeks and receiving a stable dose for at least 2 weeks, and documented HCV and HIV status. Exclusion criteria included: current pregnancy, numbness in hands that would prevent sensation of pain or movement in response to pain, and acute intoxication or psychological distress precluding participation. Participants received $50 store gift cards as compensation for time and effort involved in the in-person eligibility assessment and study visit. Written informed consent was obtained from all participants prior to study participation. The study was approved by the Institutional Review Board of Boston University Medical Campus.

2.3. Research visits/measurements

Research visits took place in the General Clinical Research Unit at Boston University School of Medicine. Participants underwent a single study visit involving a face-to-face interview assessment with a research assistant and a urine toxicology test. Participants were asked to take their normal dose of buprenorphine or methadone on the day of the study visit. The study assessment included demographics (e.g., age, education, marital status, and disability status), duration and type of opioid agonist therapy, the short form Brief Pain Inventory to assess pain (Cleeland, 2009), State Trait Anxiety Inventory (STAI; Spielberger et al., 1983, 1995) to assess anxiety symptoms, and the Patient Health Questionnaire-9 (PHQ-9; Kroenke et al., 2001) to assess depressive symptoms. The BPI assesses pain at its "worst," "least," "average," and "now" (current pain). In clinical trials, the items "worst" and "average" have each been used singly to represent pain severity; however, the scale developers recommend that all four severity items be used, because the models for validation of the BPI included all four items. The PHQ-9 is a diagnostic clinical and research tool which has been shown to be a reliable and valid measure of depression severity. It scores each of the 9 DSM-IV criteria as "0" (not at all) to "3" (nearly every day), providing a 0–27 severity score; PHQ-9 scores of 5, 10, 15, and 20 represented mild, moderate, moderately severe, and severe depression, respectively. The STAI Form is an administered analysis of reported anxiety symptoms, measuring both state and trait anxiety. The range of scores is 20–80, the higher the score indicating greater anxiety. A urine drug test using homogeneous enzyme immunoassays (Abbott/Microgenics) was conducted to assess recent use of opiates, cocaine, amphetamines, benzodiazepines, and barbiturates.

2.4. Main independent variable

The main independent variable of interest was chronic pain, defined as pain that had been present for at least 3 months. Current (past week) pain was assessed with the initial question on the Short Form Brief Pain Inventory ("During the past week have you had any bodily pain?"); persons who reported past week pain were subsequently asked about the duration of their current pain. Those who responded that their pain had been present for 3 months or longer were categorized as having chronic pain. In post-hoc analyses we evaluated a three level variable for chronic pain severity, defined as "no pain" (0), "mild pain" (1–4) and moderate to severe pain (>4). The threshold for moderate pain was the median severity score for participants with chronic pain in the sample, furthermore, it has been established as a threshold for moderate pain by other researchers (Farrar, 2010; Hoffman et al., 2010). Pain severity was assessed using the Brief Pain Inventory, rating pain from "0" (no pain) to "10" (pain as bad as you can imagine), using the mean of four responses for past week worst pain, least pain, average pain and current pain.

2.5. Dependent variables

The primary outcome was self-reporting of any opioid craving. Opioid craving was assessed using a single item numeric scale (Rosenberg, 2009). Participants were asked: "On a scale of 0–10, please indicate how much craving you have experienced during the