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Pain is not associated with worse office-based buprenorphine treatment outcomes

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Introduction

Physical pain is common among patients with opioid dependence; as many as 61% of those undergoing treatment for opioid dependence report pain lasting more than three months (1,2). There is some concern that pain might threaten substance abuse treatment success because opioid dependent patients may self-manage pain symptoms with illicit or controlled substances (3); however, studies of rapid detoxification, methadone maintenance, and residential treatment do not indicate that pain consistently negatively impacts outcomes (2,4–6).

Buprenorphine is effective for opioid addiction treatment, but may complicate pain treatment more than methadone by blocking the analgesic effects of therapeutic opioids while only providing partial opioid agonist activity (7,8). Thus, clinical guidelines state that opioid dependent patients with chronic pain may not be good candidates for buprenorphine treatment and instead recommend methadone (9). However, the impact of pain on buprenorphine treatment has not been determined in clinical studies.

We examined the association between pain and buprenorphine treatment outcomes, hypothesizing that participants with pain would have poorer treatment retention and greater opioid use than participants without pain.

Methods

Study Design

We analyzed data from a longitudinal cohort study of opioid-dependent individuals who initiated office-based buprenorphine treatment from November 2004 to December 2009 at a federally qualified health center in the Bronx, NY. Participants were followed for six months, and data collection included interviews and medical record extraction. The study was approved by the Montefiore Medical Center Institutional Review Board.

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Buprenorphine Program

Eligibility for buprenorphine followed national treatment guidelines and the program is described elsewhere in detail (10). Patients with chronic pain were not excluded from receiving buprenorphine treatment. Six general internists provided buprenorphine treatment (with buprenorphine/naloxone) and managed other medical problems, including pain. A clinical pharmacist coordinated buprenorphine care, but no substance abuse counselors, support groups, or pain management specialists were available at the health center. No participants were prescribed opioid analgesics for pain.

Subjects

Study inclusion criteria included: 1) initiation of buprenorphine treatment at the health center within 30 days or transfer from a facility within 7 days of starting buprenorphine, 2) HIV infection, and 3) English fluency. In January 2007, HIV-negative and Spanish speaking participants were also included.

Data Collection

Participants were interviewed using audio computer-assisted self-interview (ACASI) technology, prior to receiving buprenorphine treatment at the health center, and at 1, 3, and 6 months about their pain and substance use. Interviews lasted 45–60 minutes, and participants received a $15 travel reimbursement. At the end of the 6-month follow-up period, data regarding clinical visits, buprenorphine prescriptions, and medical comorbidities were extracted from electronic medical records.

Dependent Variable

Treatment retention, examined 1, 3, and 6 months after participants initiated buprenorphine treatment, was the primary outcome. Participants were categorized as retained in treatment if they had either a medical visit or active buprenorphine prescription between day 30–60 for 1-month retention, between day 90–120 for 3-month retention, and between day 180–210 for 6-month retention. Three and 6-month retention also required that participants were retained in treatment at previous time points. Self-reported use of any opioid (heroin, methadone, or opioid analgesics) in the 30 days prior to follow-up visits at 1, 3, and 6-months was the secondary outcome.

Pain Measures

The two main independent variables were “baseline pain” and “persistent pain.” The Brief Pain Inventory (BPI) asked: “Please rate your pain during the last week by selecting the one number that best describes your pain on the average” (11). Participants were given a visual analog scale from 0 to 10, with 0 labeled as “no pain” and 10 as “pain as bad as you can imagine.” Similar to prior studies, participants reporting pain scores of ≥ 5 at the initial interview were considered to have “baseline pain” (1); those reporting pain scores of ≥ 5 at all follow-up visits were considered to have “persistent pain” (5).

Other variables

Other covariates included were: age, gender, race/ethnicity, education, marriage status, employment, housing status, history of incarceration, substance use in the 30 days prior to baseline (heroin, methadone, opioid analgesics, cocaine, alcohol, sedatives, hypnotics, or tranquilizers), history of injection drug use (IDU), depressive symptoms (score of ≥ 16 from the Center for Epidemiologic Studies, Depression), and HIV status. Demographic questions were from a buprenorphine and HIV multi-site study (12), and substance use questions were from the Addiction Severity Index.

Data Analysis

We examined whether pain was associated with 6-month treatment retention using multivariate logistic regression models with retention as the dependent variable. The main independent variable was baseline pain in the first analysis and persistent pain in a second analysis. We included covariates that were associated with either pain measure (based on bivariate testing at $p<0.20$); these included depressive symptoms, history of IDU, HIV infection, and history of incarceration. Baseline sedative and alcohol use were not included in the final models due to collinearity with other measures.

We examined whether pain was associated with use of any opioids during the 6-month follow-up period using non-linear mixed effects (NLME) models with self-reported use of any opioids as the dependent variable. The NLME approach accounts for non-independence of repeated measures of opioid use within individuals. Again, the main independent variable was baseline pain in the first analysis and persistent pain in a second analysis. Each analysis adjusted for opioid use at baseline and time since initiating buprenorphine treatment. Potential confounding variables were selected as described above.

Results

Of 114 screened individuals, 108 (95%) enrolled. Of these**,** 3 withdrew, 14 did not initiate buprenorphine treatment, and 9 missed both follow-up visits (preventing determination of persistent pain and opioid use). Of 82 participants included, the median age was 45.5 years and most were male (72%), Hispanic (68%), unstably housed (60%), and had a history of IDU (51%). At baseline, 67% used heroin, 52% methadone and 26% opioid analgesics. Sixty percent had baseline pain and 38% had persistent pain. Participants with (versus without) baseline or persistent pain were more likely to have HIV infection, history of IDU, depressive symptoms, and baseline substance use (alcohol, sedative, and opioid analgesics). For those with baseline pain, over 6 months, mean pain score decreased from 7.3 to 6.0.

Buprenorphine Treatment Outcomes

Treatment retention was 91% at 1 month, 71% at 3 months, and 56% at 6 months. Retention patterns were similar in those with and without baseline or persistent pain. There was no significant association between 6-month treatment retention and baseline pain (AOR=0.81, 95% CI: 0.28–2.38, $p = 0.87$) or persistent pain (AOR=0.90, 95% CI: 0.32–2.58, $p = 0.95$) after adjustment for HIV status, depressive symptoms, history of IDU, and history of incarceration.

In the entire cohort, any opioid use decreased from 89% at baseline to 40% at 1 month, 33% at 3 months, and 26% at 6 months. Similar patterns were observed in those with and without baseline or persistent pain. We observed no significant association between any opioid use and baseline pain (AOR=1.06, 95% CI: 0.27–4.17, $p = 0.93$) or persistent pain (AOR=1.20, 95% CI: 0.31–4.63, $p = 0.79$), after adjusting for HIV status, depressive symptoms, history of IDU, history of incarceration, baseline opioid use, and time since initiating buprenorphine treatment.

Discussion

In this study of office-based buprenorphine treatment, pain was common, with 60% of participants reporting baseline pain and 38% reporting persistent pain. We found no association between pain and buprenorphine treatment outcomes, which was consistent for two measures of pain (baseline pain and persistent pain) and two buprenorphine treatment outcomes (treatment retention and self-reported opioid use). Participants with and without

pain achieved treatment success; 56% were retained in treatment at 6 months and opioid use decreased from 89% to 26%.

The lack of an association between pain and treatment outcomes contradicts the findings of some previous studies that were conducted in other treatment settings. Cross sectional studies of methadone maintenance and drug-free residential or outpatient programs found an association between pain and weekly heroin use (1,2). Prospective studies of detoxification programs demonstrated higher rates of ongoing heroin use in those with versus without persistent pain (4,5). However, a prospective study of treatment with methadone or levo-alpha-acetyl-methadol reported results similar to ours (6), although to our knowledge, our study is the first to evaluate the relationship between pain and treatment outcomes in office-based buprenorphine treatment. These findings suggest that treatment modality may be important for patients with opioid dependence and pain, and opioid replacement therapy with buprenorphine or methadone may attenuate the negative impact of pain on treatment outcomes that has been reported in detoxification or drug-free settings.

It is possible that study participants with pain derived some analgesia from buprenorphine treatment, which could have limited the negative impact of pain on treatment outcomes. This is supported by our finding that study participants with baseline pain had a reduction in mean pain scores over six months. However, additional research is needed to determine whether buprenorphine treatment can be optimized for the treatment of both pain and opioid dependence.

One limitation of our study was the relatively small sample size. Another limitation was our inability to validate our secondary treatment outcome of self-reported opioid use, e.g., with urine drug testing. Finally, our study took place in a single community health center serving a marginalized urban population, which may limit generalizability.

To our knowledge, this is the first study to prospectively evaluate the association between pain and office-based buprenorphine treatment outcomes. While the findings need to be confirmed by larger studies, opioid-dependent participants with pain had similar buprenorphine treatment outcomes to those without pain. These findings should reassure clinicians that good buprenorphine treatment outcomes can be achieved in patients with opioid dependence and pain.

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