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Longitudinal Analysis of Pain and Illicit Drug Use Behaviors in Outpatients on Methadone Maintenance*

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Abstract

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Contributors

All authors have participated sufficiently in the work to take responsibility for authorship and publication. Lara Dhingra, Russell Portenoy, Martin Cheattle, David Perlman, and Carmen Masson made substantial contributions to the design, data collection, analysis, and writing of the manuscript. Jack Chen, Courtney McKnight, and Ashly Jordan made substantial contributions to the data collection and preparation and literature review. Tom Wasser made substantial contributions to the data analysis. All authors contributed to interpreting the results and have approved the final manuscript.

Conflict of Interest

No conflict declared

Note: The findings and conclusions in this article are those of the authors and do not necessarily represent the views of the National Institute on Drug Abuse or National Institutes of Health.

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Background—Little is known about the experience of chronic pain and the occurrence of illicit drug use behaviors in the population enrolled in methadone maintenance treatment (MMT) programs.

Methods—This is a secondary analysis of longitudinal data from two MMT samples enrolled in a randomized controlled trial of hepatitis care coordination. Patients completed pain, illicit drug use, and other questionnaires at baseline and 3, 9, and 12 months later. Associations were sought over time between the presence or absence of clinically significant pain (average daily pain ≥ 4 or mean pain interference ≥ 4 during the past week) and current illicit drug use (i.e., non-therapeutic opioid, cocaine or amphetamine use identified from self-report or urine drug screening).

Results—Of 404 patients providing complete data, within-patient variability in pain and illicit drug use was high across the 4 assessment periods. While 263 denied pain at baseline, 118 (44.9%) later experienced clinically significant pain during 1 follow-up assessments. Of 180 patients (44.6%) without evidence of illicit drug use at baseline, only 109 (27.0%) had similar negative drug use at all follow-up assessments. Across four assessment periods, there was no significant association between pain group status and current illicit drug use.

Conclusions—This one-year longitudinal analysis did not identify a significant association between pain and illicit drug use in MMT populations. This finding conflicts with some earlier investigations and underscores the need for additional studies to clarify the complex association between pain and substance use disorders in patients in MMT program settings.

Keywords

pain; methadone maintenance; addiction; illicit drug use; pain management

1. INTRODUCTION

Surveys suggest that 37%–80% of the 301,551 (SAMHSA, 2013) patients receiving methadone maintenance treatment (MMT) in the U.S. have clinically significant chronic pain (Barry et al., 2009a; Dhingra et al., 2013; Jamison et al., 2000; Nielsen et al., 2013; Peles et al., 2011, 2005; Pud et al., 2012; Rosenblum et al., 2007, 2003; Trafton et al., 2004). Studies in these and other populations with substance use disorders (SUDs) suggest that unrelieved pain may be linked to poorer addiction-related outcomes (Brennan et al., 2005; Caldeiro et al., 2008; Larson et al., 2007; Peles et al., 2005; Potter et al., 2008; Pud et al., 2012; Rosenblum et al., 2003; Sheu et al., 2008; Trafton et al., 2004; Weiss et al., 2014). These associations, which raise concerns about the possibility that unrelieved pain or its consequences may trigger illicit drug use, have not been confirmed by other surveys showing no such association (Barry et al., 2009a, 2009b; Dhingra et al., 2013; Nielsen et al., 2013). Further studies are needed to clarify the potential linkages between pain experience and illicit drug use behaviors.

A hepatitis care coordination trial provided an opportunity for a secondary analysis of pain-related data from two MMT programs (Masson et al., 2013; Perlman et al., 2014; Dhingra et al., 2013; Larios et al., 2014). Cross-sectional baseline data from this study revealed no statistically significant association between pain and illicit drug use behaviors (Dhingra et al., 2013). The one-year longitudinal follow-up data provided an opportunity for a more

robust examination of this relationship. The Institutional Review Boards at Mount Sinai Beth Israel and the University of California in San Francisco approved the analysis.

2. METHODS

2.1. Patient Selection and Procedures

Patients in New York City and San Francisco who were enrolled in two MMT programs participated in a one-year randomized controlled trial of a hepatitis prevention intervention. Selection criteria, enrollment procedures, study interventions, and primary outcomes have been described previously (Dhingra et al., 2013; Larios et al., 2014; Masson et al., 2013; Perlman et al., 2014). All patients completed measures at baseline and 3, 9, and 12 months later.

2.2. Measures

Pain and illicit drug use were assessed at each time point. The Brief Pain Inventory-Short Form (BPI-SF) was used to measure pain intensity and pain interference in function during the past week (Cleeland, 2009; Daut et al., 1983; Keller et al., 2004; Mendoza et al., 2006). Pain intensity “on average” is measured on a 0–10 numeric scale and pain interference in each of 7 functional domains (e.g., general activity; walking; work; mood; sleep, etc.) is measured on separate 0–10 numeric scales, the average of which is a pain interference index (Cleeland, 2009). Information is queried about pain treatments, including current analgesic medications, psychological treatments, and complimentary and alternative medicine (CAM) treatments. Additional CAM treatments previously recognized by the National Center for CAM (2010) were also assessed. Current illicit drug use was assessed by urine drug screening (UDS) and by self-report using the drug use subscale (Zanis et al., 1994) of the Fifth Edition of the Addiction Severity Index (ASI) (McLellan et al., 1992).

2.3. Statistical Analyses

At each time point, patients were categorized as having “no pain,” “non-clinically significant pain,” or “clinically significant pain (CSP).” Those who screened negatively for pain or indicated on the BPI-SF that they had “0” pain “on average” during the past week were considered to have no pain. Those with average daily pain ≥ 4 or mean pain interference ≥ 4 during the past week were considered to have CSP. Patients with pain who did not meet these criteria were considered to have non-clinically significant pain.

Patients were similarly categorized in terms of illicit drug use at each time point. Current illicit drug use was defined as a positive UDS result for opioids other than methadone if the patient did not report using a prescribed opioid for pain, a positive UDS result for cocaine or amphetamines, or self-reported use of heroin, cocaine or amphetamines on any of the past 30 days.

All analyses were performed in SPSS version 22.0. Sociodemographic variables were compared across the no pain, non-clinically significant pain, and CSP groups using chi-square tests for discrete variables and analysis of variance (ANOVA) for continuous data. For significant ANOVAs, post-hoc testing was performed with the Scheffe procedure.

Comparisons between the presence or absence of CSP at each time point (Yes/No) and the presence or absence of current illicit drug use at each time point (Yes/No) were assessed using chi-square analysis. Any $p < 0.05$ was considered to be statistically significant. Due to the exploratory nature of this analysis, no corrections were applied to the p-values for multiple comparisons.

3. RESULTS

Baseline and longitudinal analyses used the total enrolled sample of 404 patients who provided complete data for the 1-year study period. The mean age was 45.4 years ($SD = 9.8$); 32.7% were women, and 34.7% were Non-Hispanic white. At baseline, 263 (65.1%) patients had no pain, 37 (9.2%) had non-clinically significant pain, and 104 (25.7%) had CSP. Patients with CSP were significantly older, more likely to be married, were enrolled in MMT longer, and had higher methadone dosages than those without pain ($p = 0.013, 0.006, 0.046$ and 0.005 respectively). There were no other baseline differences among these groups in sociodemographic characteristics. Patients with CSP used more prescribed opioids (38.5%), prescribed non-opioids (22.1%), and over-the-counter analgesics (47.1%) than those with non-clinically significant pain (24.3%, 16.2%, and 43.2% respectively) or no pain (9.9%, 3.0%, and 22.8%, respectively; all $p < 0.001$) (Table 1a).

Among patients with CSP at baseline, 19 (18.3%) endorsed non-therapeutic opioid use, 44 (42.3%) cocaine use, and 2 (1.9%) amphetamine use in the past 30 days. Current UDS results for opioids, cocaine, or amphetamines were 39.4%, 42.3%, and 1.9%, respectively. These self-reported illicit drug use and UDS results did not differ by pain status (Supplementary Table¹).

Pain status fluctuated greatly over the course of one year of follow-up. A total of 125 of the 404 patients (30.9%) had unchanging pain status across all 4 time points; this included 48 (11.9%) with no pain, only 12 (3.0%) with non-clinically significant pain, and 65 (16.1%) with CSP. All other patients shifted pain status one or more times during the course of the year. For example, while 263 patients denied having pain at baseline, 118 (44.9%) of these patients later experienced CSP during 1 or more subsequent follow-up periods. Similarly, patients shifted between current illicit drug use and no use across time points. Based on self-report or UDS, 228 (56.4%) of patients had unchanging illicit drug use across all 4 time points (119 [29.5%] with illicit drug use during all 4 time periods and 109 [27.0%] with no evidence of illicit drug use across all 4 time points). Additionally, the highest rate of non-therapeutic opioid use was at baseline (24.5%) and the lowest rate was at 9 months (18.8%). The highest and lowest rates for cocaine, and amphetamines, respectively were 40.8% at baseline vs. 36.4% at 12-months, and 5.9% at 3-months vs. 3.2% at baseline.

Associations between episodes of CSP and current illicit drug use events for each of the 4 assessment periods were not statistically significant (all $p > 0.13$). Further, there was no statistically significant association between the number of CSP episodes over 12 months and

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the number of current illicit drug use events ($p = 0.691$; Table 1b). Inspection of the distributions of the two variables revealed no identifiable pattern (Figure 1).

4. DISCUSSION

This analysis revealed no association between episodes of CSP and the occurrence of current illicit drug use over the course of one year in a large and diverse group of patients enrolled in one of two MMT programs. This finding confirms the analysis of baseline data from the same study (Dhingra et al., 2013) and is consistent with several other published cross-sectional studies of chronic severe pain and pain of varying severity (Barry et al., 2009a, 2009b; Nielsen et al., 2013). For example, a cross-sectional study of 251 veterans undergoing agonist therapy found that only self-reported recent marijuana use, but not heroin use, was associated with moderate to severe pain of unspecified duration (Trafton et al., 2004). A recent cross-sectional study in 277 MMT outpatients found that only positive UDS results for benzodiazepines, including those used therapeutically, but not opioids or cocaine, was associated with pain of unspecified duration and intensity (Dunn et al., 2014). Given the lack of data on current marijuana and benzodiazepine use in the present study, comparisons with earlier studies are limited.

Other studies have yielded conflicting data, which together suggest a link between poorly controlled pain and illicit drug use behaviors (Brennan et al., 2005; Caldeiro et al., 2008; Larson et al., 2007; Peles et al., 2005; Potter et al., 2008; Rosenblum et al., 2003; Sheu et al., 2008; Weiss et al., 2014). One longitudinal study, for example, revealed that persistent moderate to severe pain was a predictor of recurrent alcohol and opioid abuse in 397 patients who were evaluated over a 2-year period following treatment in a residential detoxification program (Larson et al., 2007). Another longitudinal study found that moderate to severe pain was associated with more problematic drinking in 227 older adults with pre-existing alcohol use problems (Brennan et al., 2005). Comparisons with these two latter studies are limited as the current study did not assess alcohol. Similarly, a longitudinal study of 582 veterans in addiction treatment showed that those with moderate to severe chronic pain had poorer retention and 12-month abstinence rates vs. those with none to mild pain (Caldeiro et al., 2008), and a cross-sectional analysis of 7,876 patients with various SUDs in 4 treatment settings showed that individuals with moderate to severe pain were more likely to report heroin use than those with mild pain or no pain (Potter et al., 2008). Finally, a cross-sectional survey of 170 MMT patients in Israel found that individuals with chronic moderate to severe pain were more likely to have positive UDS results for benzodiazepines at levels suggestive of abuse than those without pain (Peles et al., 2005). Other studies have observed that patients with pain and substance use disorders often report using substances to self-medicate for their pain (Barry et al., 2009b; Rosenblum et al., 2003; Sheu et al., 2008). Additional investigations are needed to understand the nature of these contradictory data and determine whether the relationship observed in some surveys is prominent only in specific subgroups of patients and clinically important in any. To date, all data are correlative and there is no evidence that there is a causal relationship between pain and substance use in the MMT population.

In the current study, patients' pain status and current illicit drug use fluctuated greatly over the course of one year. In contrast, a national survey of 200 MMT patients ($n=103$) observed little within-patient variability in pain over 1 year (Ilgen et al., 2006). Few longitudinal data on the prevalence of pain in MMT populations are available, thus, comparisons are limited. We also found that patients with CSP were significantly older, more likely to be married, were enrolled in MMT longer, and had higher methadone dosages than those without pain. The finding that higher methadone dose was associated with chronic severe pain was noted in an earlier study (Peles et al., 2005). It may suggest that patients with more severe SUDs are more likely to have more severe pain, or that higher methadone doses reflected an effort to provide concurrent pain treatment. Once daily methadone is not an effective strategy for pain (Dhingra et al., 2013), and if the higher dose in MMT did reflect a concern about pain, it may suggest a need for pain education for MMT professionals and better access to pain care for patients. Additional studies are needed to explain this finding.

This study has limitations. It is a secondary analysis and important characteristics about pain, such as duration, were not assessed. Little detail was available about pain treatment, including prescribed opioids, and data pertaining to pain's association with marijuana and alcohol use and the use of substances to self-medicate pain were lacking. Nonetheless, the study provides a longitudinal, prospective evaluation of a subset of patients in two large MMT programs using standardized validated instruments to assess pain and other outcomes, the use of self-report and objective measurements of current illicit drug use, and data from a diverse sample. The analysis contributes both new and confirmatory data to the conflicting literature on the complex and still unelucidated association between chronic pain and SUDs and suggests areas for further investigation.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- Pain and illicit drug use were evaluated in methadone-maintained patients.
- There was no significant association between pain and illicit drug use.
- Within-patient variability in pain and illicit drug use was high over 1 year.
- These findings conflict with earlier studies in methadone-maintained patients.

Figure 1.

Illicit drug use events by number of clinically significant pain episodes over 12 months in outpatients undergoing methadone maintenance ($n = 404$).

Abbreviation: CSP = Clinically significant pain; Illicit drug use events defined as positive drug screen for opiates, cocaine or amphetamines, or self-reported use over the past 30 days.

Table 1aUse of pain treatments in outpatients on methadone maintenance at baseline ($n = 404$)

Characteristic	No Pain		Non-Clinically Significant Pain		Clinically Significant Pain		Chi-Square p-value
	N	%	N	%	N	%	
Prescribed opioid analgesics ^a	26	9.9	9	24.3	40	38.5	< 0.001
Prescribed non-opioid analgesics ^a	8	3.0	6	16.2	23	22.1	< 0.001
Over-the-counter-analgesics ^a	60	22.8	16	43.2	49	47.1	< 0.001
Prayer ^b	13	4.9	3	8.1	9	8.7	0.363
Vitamins/dietary supplements ^b	0	0	0	0	0	0	N/A
Distraction techniques ^a	13	4.9	5	13.5	17	16.3	0.001
Relaxation techniques ^a	13	4.9	5	13.5	13	12.5	0.019
Herbal medications/supplements ^b	3	1.1	0	0.0	3	2.9	0.339
Massage ^b	8	3.0	2	5.4	10	9.6	0.032
Acupuncture/acupressure ^b	5	1.9	1	2.7	5	4.8	0.305
Aromatherapy ^b	2	0.8	0	0.0	2	1.9	0.488
Homeopathy ^b	2	0.8	2	5.4	1	1.0	0.055
Chiropractic ^b	2	0.8	0	0.0	2	1.9	0.488
Reflexology ^b	0	0.0	0	0.0	2	1.9	0.055
Energy healing ^b	2	0.8	0	0.0	1	1.0	0.841
Biofeedback training ^a	2	0.8	1	2.7	1	1.0	0.535
Hypnosis ^a	0	0.0	1	2.7	1	1.0	0.066
Warm compress ^a	12	4.6	8	21.6	21	20.2	< 0.001
Cold compress ^a	7	2.7	4	10.8	10	9.6	0.007
Other ^c	1	0.4	1	2.7	5	4.8	0.012

^aFrom the Brief Pain Inventory-Short Form.^bMeasured in the past 30 days.

Including exercise; braces; physical therapy; vibrating electrode; topical ointments; and meditation.

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Number of illicit drug use events and clinically significant pain episodes over 12 months in outpatients undergoing methadone maintenance ($n = 404$)

Table 1b

	Number of Clinically Significant Pain Episodes					Total
	0	1	2	3	4	
0	39	14	24	15	18	110
1	21	8	12	6	6	53
2	22	15	8	8	11	64
3	28	5	9	8	9	59
4	49	19	16	13	21	118
Total	159	61	69	13	21	404

($p = 0.691$); Illicit drug use events defined as positive drug screen for opiates, cocaine or amphetamines, or self-reported use over the past 30 days.