American Pain Society
RESEARCH
EDUCATION
TREATMENT
ADVOCACY
PUBLISHED BY ELSEVIER

The Journal of Pain, Vol 16, No 9 (September), 2015: pp 887-894
Available online at www.jpain.org and www.sciencedirect.com

Pain Among High-Risk Patients on Methadone Maintenance Treatment

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Abstract: The complexity of treating concurrent pain and opioid dependence among many methadone-maintained individuals presents a major challenge in many clinical settings. Furthermore, recent expert guidelines have called for increased research on the safety of methadone in the context of chronic pain. This study explores the prevalence and correlates of pain among a prospective cohort of people who use illicit drugs in Vancouver, British Columbia, Canada, who reported enrollment in methadone maintenance treatment (MMT) between 2011 and 2014. Among the 823 participants eligible for this analysis, 338 (40.9%) reported moderate pain and 91 (11.1%) reported extreme pain at the first study visit. In multivariable, generalized, linear mixed model analyses, higher pain severity was positively and independently associated with self-managing pain (adjusted odds ratio [AOR] 2.15, 95% confidence interval [CI] 1.77–2.60), patient perception of methadone dose being too low (AOR 1.82, 95% CI 1.41–2.34), older age (AOR 1.31, 95% CI 1.13–1.51), having a physical disability (AOR 4.59, 95% CI 3.73–5.64), having ever been diagnosed with a mental illness (AOR 1.44, 95% CI 1.13–1.84), white ethnicity (AOR 1.42, 95% CI 1.10–1.83), and marijuana use (AOR 1.25, 95% CI 1.02–1.52). These findings suggest several areas for clinical intervention, particularly related to patient education and alternative analgesic approaches for MMT patients experiencing pain.

***Perspective:** To better understand the complexity of concurrent pain and opioid dependency among individuals on methadone maintenance treatment, this article describes the prevalence and correlates of higher pain severity among methadone-maintained people who use illicit drugs. Patients on methadone with comorbid pain may benefit from education and alternative analgesic approaches.*

***Key words:** Pain, methadone, substance abuse, self-medication, opioid-induced hyperalgesia.*

Received April 24, 2015; Revised May 28, 2015; Accepted June 6, 2015.
Conference presentation: Part of these data appeared as a poster presentation at the American Pain Society's 34th Annual Scientific Meeting, Palm Springs, CA, May 13–16, 2015.
Disclosures: This study was supported by the U.S. National Institutes of Health (R01DA011591 and R01DA021525). This research was undertaken, in part, thanks to funding from the Canada Research Chairs program through a Tier 1 Canada Research Chair in Inner City Medicine, which supports E.W. J.M. is supported with grants paid to his institution by the British Columbia Ministry of Health and by the U.S. National Institutes of Health (R01DA036307). He has also received limited unrestricted funding, paid to his institution, from Abbvie, Bristol-Myers Squibb, Gilead Sciences, Janssen, Merck, and ViiV Healthcare. P.V. and K.H. are supported by the Canadian Institutes of Health Research. The authors have no other potential competing interests to declare.
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1526-5900/$36.00

http://dx.doi.org/10.1016/j.jpain.2015.06.003

Methadone is a long-acting opioid agonist that may be prescribed to treat opioid dependence or chronic pain. When treating opioid-dependent individuals, clinicians are often faced with the complex challenge of treating concurrent chronic pain, which is estimated to be prevalent among 55 to 61% of individuals on methadone maintenance treatment (MMT) compared with 31% of the general adult population.[14]

The physiological mechanisms that may explain the overlap between pain and opioid dependency remain a topic of ongoing debate. One hypothesis that has garnered significant attention is the notion of opioid-induced hyperalgesia, which suggests that consistent exposure to opioids may lead to increased pain sensitivity, decreased pain thresholds, or both. However,

limited and conflicting evidence has precluded a consensus on this hypothesis.[1,15]

The complexity of concurrent pain and opioid dependence presents substantial challenges for both clinicians and patients. Often, it is difficult to achieve a balance between adequate pain relief and reduced opioid cravings, while at the same time minimizing the risks of deepened dependence, overdose, withdrawal, misuse, or diversion.[23] Furthermore, practitioners' treatment decisions may be influenced by stigma related to people who use illicit substances,[34] interpretations of requests for opioids as drug seeking,[2] or views of MMT as a treatment of either pain or addiction separately.[22] These factors may contribute to inadequate pain management among individuals with high rates of disability and other causes of chronic pain.

In addition to these issues, recent guidelines by the American Pain Society call for increased research on the safety of methadone among individuals with chronic pain.[8,45] Therefore, we undertook this study to investigate the prevalence and correlates of pain among opioid-dependent individuals on MMT to inform pain management and risk mitigation strategies among this particularly high-risk population.

Methods

Study Design and Setting

Data for these analyses were derived from 2 ongoing prospective observational cohorts in Vancouver, British Columbia, Canada: the ACCESS (AIDS Care Cohort to Evaluate Exposure to Survival Services) of human immunodeficiency virus (HIV)-seropositive illicit drug users and the VIDUS (Vancouver Injection Drug Users Study) of HIV-seronegative injection drug users. These cohorts have previously been described in detail and have received annual ethics approval from the University of British Columbia and Providence Health Care Research Ethics Board.[39,40] Since 1996, more than 2,000 participants have been recruited into these cohorts through snowball sampling and street outreach methods in Vancouver's Downtown Eastside (DTES). The DTES is a postindustrial neighborhood with an established drug market and widespread illicit drug use, poverty, poor housing conditions, and infectious diseases such as HIV and hepatitis C.[26] The present analyses were restricted to interviews that were conducted between December 1, 2011, and November 30, 2014. These dates coincided with the start of the EuroQol EQ-5D health utility instrument in the study questionnaire and included all subsequent follow-up data available at the time of data analysis.

Participants

Participants are eligible for VIDUS if they are 18 years of age or older and have injected an illicit drug in the month before the baseline interview. Participants are eligible for ACCESS if they are HIV seropositive, are 18 years of age or older, and have used an illicit drug other than cannabinoids within the month before the baseline interview. At baseline and semiannually, participants answer an interviewer-administered questionnaire and provide blood samples for serologic analysis (HIV-negative individuals) or disease monitoring (HIV-positive individuals) and are referred as necessary to medical care and drug and alcohol treatment. All participants provide written informed consent and receive a $30 stipend at the end of each study visit. Participants were eligible for this analysis if they reported being on MMT at the time of their interview.

Variables and Measures

To identify factors associated with pain among individuals enrolled in MMT, our outcome of interest was current pain severity, which was measured using ordinal multinomial categories of participants who reported no pain or discomfort, moderate pain or discomfort, or extreme pain or discomfort at the time of their interview. These data on pain severity were ascertained using the EuroQol EQ-5D health utility instrument, which has been shown to be a valid, responsive, and reliable instrument for individuals with pain and opioid dependence.[18,30,43] In addition, the Brief Pain Inventory (BPI) Short Form was used to elicit information on pain duration and interference. The BPI has been shown to be a valid and reliable self-reported pain instrument, which has been widely used in studies measuring pain among general and substance-using populations.[6,31,35] Because the BPI was introduced later in the study period, data on these additional pain measures are available only for participants who completed the most recent follow-up period from June 1, 2014, to November 30, 2014.

The self-reported demographic, behavioral, social, and structural explanatory characteristics considered in the analyses were age (per 10-year increase), gender (male vs female), ethnicity (white vs other), homelessness (yes vs no), residence in Vancouver's DTES neighborhood (yes vs no), highest education status obtained ($\geq$ high school diploma or equivalent vs < high school diploma), HIV serostatus (positive vs negative), hepatitis C status (positive vs negative), lifetime history of mental illness diagnosis (yes vs no), incarceration (yes vs no), physical disability (yes vs no), self-managed pain (yes vs no), and having been denied pain medication by a health practitioner (yes vs no). The variables related to methadone treatment or drug use included nonfatal overdose (yes vs no), current methadone dose (per 10 mg/d increase), methadone dose perceived to be too low (yes vs no), any illicit methadone injection (yes vs no), any crack cocaine use (yes vs no), any crystal methamphetamine injection (yes vs no), any heroin injection (yes vs no), any cocaine injection (yes vs no), any marijuana use (yes vs no), any heavy alcohol use (yes vs no), any prescription opioid misuse (yes vs no), and any binge injection drug use (yes vs no). As per the National Institute on Alcohol Abuse and Alcoholism, heavy alcohol use was defined as more than 4 drinks per day or more than 14 drinks per week for men or more than 3 drinks per day or more than 7 drinks per week for women.[28] Prescription