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Correlates of pain in an in-treatment sample of opioid-dependent people

Abstract

Introduction and Aims The limited literature on pain in opioid-treatment samples indicates that it is highly prevalent. Understanding the implications of pain on treatment outcomes is important, particularly in light of ageing opioid-treatment cohorts. This study explores correlates of pain, including aberrant behaviours related to prescribed opioids. Our hypothesis is that pain may increase aberrant opioid-related behaviours, including illicit substance use, among opioid-dependent people. **Design and Methods** We examined pain in methadone or buprenorphine patients (n = 141) from three treatment services. Measures included basic demographics, Brief Pain Inventory, general mental health, physical health and quality of life measures, pain history and treatments, and an aberrant opioid-related behaviour scale. Univariate and multivariate analyses were used to examine correlates of pain. **Results** Forty percent reported current pain, measured with the first question of the Brief Pain Inventory. Correlates of pain were depression ratings [adjusted odds ratio (OR) 2.24, 95% confidence interval (CI) 1.04, 4.83], anxiety ratings (adjusted OR 4.29, 95% CI 1.88, 9.80) and self-reported health ratings (adjusted OR 0.35, 95% CI 0.16, 0.76). Contrary to our hypothesis, pain was not associated with greater use of illicit opioids, nor any aberrant opioid-related behaviours. Pain was comparable among methadone and buprenorphine patients. **Discussion and Conclusions** The lack of association with pain and aberrant behaviours suggest that it should not be assumed that those in opioid treatment misuse medications in response to pain. The high prevalence of depression/anxiety symptoms indicates a need for further work with larger samples to explore pain and co-morbidity among opioid-dependent people.

Keywords

pain, correlates, in-treatment, people, sample, opioid-dependent

Disciplines

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Running title: Pain in Opioid Substitution Treatment

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Abstract

Abstract

Introduction: The limited literature on pain in opioid treatment samples indicates that it is highly prevalent. Understanding the clinical implications of pain on treatment outcomes is important, particularly in light of ageing opioid-treatment cohorts. This study explores correlates of pain, including aberrant behaviors related to prescribed opioid use. Our hypothesis is that pain may increase aberrant opioid-related behaviors, including illicit substance use, amongst opioid-dependent people.

Methods: We examined pain, physical health and treatments tried in methadone or buprenorphine patients (n = 141) from three treatment services. Measures included basic demographics, the Brief Pain Inventory, general mental health, physical health and quality of life measures, pain history and an aberrant opioid-related behaviors scale. Univariate and multivariate analysis were used to examine correlates of pain.

Results: Forty percent of the sample reported current pain, measured with the first question of the brief pain inventory. Correlates of pain were depression ratings (AdjOR: 2.24, 95%CI: 1.04, 4.83)/anxiety ratings (AdjOR: 4.29, 95%CI: 1.88, 9.80) and poorer ratings of health (AdjOR: .35, 95%CI: .16, .76). Contrary to our hypothesis, pain was not associated with greater use of illicit opioids, nor with any aberrant opioid-related behaviors. Pain was comparable amongst methadone and buprenorphine treatment participants.

Discussion and conclusions: The lack of association with pain and aberrant behaviors suggest it should not be assumed that those in opioid treatment misuse medications in response to pain. The high prevalence of depression/anxiety symptoms suggests a need for further work with larger samples to explore pain and co-morbidity amongst opioid dependent people.

Key words: pain, opioid substitution treatment, methadone, buprenorphine

Introduction

Despite a need for research in the complex area of pain amongst opioid-dependent people, there has been little systematic examination of pain prevalence in this population.

Most of the current literature has come from North America, and is limited to methadone patients. Among such samples, pain has been reported to be highly prevalent, with pooled estimates of 82% (95%CI 76,87) reporting recent pain (1, 2), and pooled estimates of 38% (95%CI 23,55) reporting chronic or chronic severe pain (2-4).

Pain management amongst opioid-dependent people is a difficult area (5-7). The complexity amongst those in opioid substitution treatment (OST) programs is complicated by: the unique pharmacological profiles of partial-agonist buprenorphine; hesitancy to prescribe pain medication where opioid dependence exists; and opioid-induced hyperalgesia that may impair ability to manage pain in OST patients (8-10). These factors, combined with an ageing populations of opioid-dependent people (11-13), mean that research is required to better understand pain in this population.

Studies have also found that pain is associated with comorbidities such as depression and disordered sleep (14), and the use of other substance use such as benzodiazepines (3), unsanctioned pharmaceutical opioids and heroin (1), which may also negatively impact on treatments. Findings regarding OST dose and pain have been mixed. One study found significantly higher doses in patients with pain (3), while another study found no association (2). Age, sex and time in treatment have also been associated with pain amongst methadone patients (1, 2, 4).

The aim of this study is to add to the limited international literature on current pain prevalence and correlates of pain in OST populations. In addition, the study examines the

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relationship between current pain and aberrant drug related behaviors. Our hypothesis is that current pain may add to the occurrence of aberrant opioid-related behaviors, including illicit substance use, amongst opioid dependent people.

Methods

Participants

Participants (n = 141) were recruited from three OST programs (2 public, 1 private), in Sydney and Newcastle, Australia. Sample characteristics are found in Table 1.

Procedures

Recruitment occurred from May to November 2011 through study advertisements placed in OST clinics. After signing the informed consent, eligible participants self-completed the survey with researcher available to answer questions.

Participants received \$30 for time and expenses incurred. Ethical approval was granted by the appropriate New South Wales Health Human Research Ethics Committees (HRECs) and University of New South Wales HREC.

Assessments

The survey included demographics, general health, use of pain treatments, pain severity and interference (Brief Pain Inventory Short Form)(15); mental health and wellbeing (including the Depression Anxiety Stress Scales, where the cut-offs for “severe” and “extremely severe” Depression/Anxiety symptomology were used, as per the DASS manual)(16), alcohol and other drug use (risky alcohol drinking, defined as a cut-off ≥ 4 on the Alcohol Use Disorders Identification Test (AUDIT-C) (17), and quality of life (WHO Quality of Life Scale (WHOQOL-Bref)(18) .

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Current pain was determined by a positive response to the first question on the BPI: “Throughout our lives, most of us have had pain from time to time (such as minor headaches, sprains, and toothaches). Have you had pain other than these everyday kinds of pain today?”

Aberrant (or “divergent”) opioid-related behaviors were measured using the Opioid Related Behaviours in Treatment (ORBIT) scale (19), developed for use among Australian patients receiving chronic opioid therapy (for pain or opioid dependence) in both clinical and research settings. The scale has demonstrated strong internal consistency (Cronbach alpha = 0.85).

Analyses

Descriptive statistics were used to describe the sample. To determine which characteristics were individually associated with the current pain, items were individually entered into binary logistic and regression models. Where characteristics were associated with pain, they were entered into a multivariate model to determine if current pain predicted any of these treatment or health outcomes after controlling for demographic (age and gender) and treatment characteristics (type of OST and length of time in treatment). Given the sample size, some effects fell short of traditional levels of statistical significance. To protect against placing undue weight on ‘trend’ level effects (which may arise from Type I errors), effect sizes were calculated using Hedges’ g . This statistic can be interpreted in a similar fashion to the more common Cohen’s d , but has less positive bias with small samples (20, 21). ‘Trend’ level effects ($0.1 > p > 0.05$) are only interpreted where the magnitude of effect was moderate or greater ($g \geq 0.5$), which suggests meaningful differences are apparent.

Results

Participants

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The demographic characteristics of the sample appeared broadly representative of OST clients in Australia, being around two thirds male, largely unemployed, and with 70% being prescribed methadone (11).

INSERT TABLE 1 around here

Pain and OST Type

No difference was observed in the reporting of current pain between those receiving methadone (41%) and those receiving buprenorphine (40%). The mean scores indicated moderate pain severity and interference in both groups. There was no difference in the mean pain severity score in methadone (4.6, SD 2.4) and buprenorphine (4.7, SD 2.3; Hedges' $g=0.04$) patients or mean pain interference score in methadone (5.5, SD 2.8) or buprenorphine (5.4, SD 2.4; $g=0.04$).

Dose comparisons for those with current pain

The association with methadone dose and pain severity amongst those with pain did not reach significance ($r(31) = .348, p = .055$); no association was found for buprenorphine ($r(15) = .166, p = .554$).

Dose comparisons between those with and without current pain

There was a trend for those with pain to have a higher mean buprenorphine dose (mean 19.0mg, SD 9.7mg) compared to those without pain (13.7mg, SD 5.9), $t(20.5) = -1.884, p = .074, g=0.68$. No association was seen with methadone dose and current pain ($t(74) = .379, p = .706$).

Pain treatments tried

Most (68%) of the sample that reported pain also reported that they had tried some non-opioid type pain interventions for their pain. The most common interventions reported were non-opioid medications ($n = 28, 49%$, with the most common medications reported being

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anti-inflammatories, $n = 8$, and paracetamol, $n = 6$), meditation ($n = 12$, 19%), relaxation techniques ($n = 10$, 18%), seeing a psychiatrist ($n = 7$, 12%), seeing a counselor ($n = 6$, 11%), or physiotherapy ($n = 6$, 11%).

Correlates of pain

Those reporting current pain were compared with those that did not report current pain.

Univariate analysis revealed no difference in time in treatment for those with current pain to and those without current pain ($p = .079$, 226 weeks compared with 120 weeks, $g=0.31$).

Those with current pain were more likely to report severe to extremely depression/anxiety ratings on the DASS (Table 2). In addition, those with current pain were less likely to rate their own health as good to excellent (46% compared with 71%), and score lower on the Physical component score of the WHOQoL (Mean of 53.7 for those without pain compared with mean of 42.0 for those with pain, $g=0.66$). As shown by the adjusted odds ratios reported in Table 2, these associations remained significant after controlling for age, gender, type of opioid treatment and length of time in opioid, indicating that current pain is independently associated with depression/anxiety ratings, and poorer ratings of physical health.

Other substance use, including heroin and illicit prescription opioid use, benzodiazepine use and risky alcohol use were not associated with current pain.

Pain was not associated with increased endorsement of any of the individual aberrant behaviours examined, nor the total number of behaviours that were endorsed.

INSERT TABLE 2 AROUND HERE

Discussion

This study examined current pain, and correlates of pain amongst a sample of opioid-dependent people, adding to the limited literature in this area, including a novel aspect of examination of aberrant behaviors and pain amongst an opioid substitution treatment sample. While we found lower levels of current pain than had been described in other samples of methadone patients, those in pain had high levels of severe psychiatric morbidity, which has important implications for treatment planning.

Interestingly there was no association with pain and illicit use of prescription opioids or reporting of aberrant opioid-related behaviors, suggesting in this sample of OST patients, pain was not leading to an increase in the aberrant behaviors we measured in this study, such as attending multiple prescribers, medication sharing or early script renewal requests. The lack of association between current pain and illicit prescription opioid use is consistent with previous work finding that those chronic pain did not use more heroin or non-prescribed prescription opioids (22), and in contrast with the hypothesis that current pain may contribute to the prevalence of aberrant opioid-related behaviors including substance use. This result may be associated with the finding that most of this in-treatment sample reported trying non-opioid treatments for pain, therefore were willing and able to access a range of health care interventions to address their pain conditions. Although it is not possible to confirm this from the data available, this would be an important area for future work.

Some correlates of pain were consistent with those reported in other studies (2, 4, 14) with depression and poorer ratings of physical health associated with current pain.

An association was seen with mental health comorbidity and poorer self-rating of health amongst patients reporting current pain. While the association with mental health and pain is well known, this is still an important reminder that amongst opioid-dependent people, existence of current pain may also indicate a need to screen for other comorbidities including depression and anxiety. Around half the participants who reported pain met the cut-off for severe or extremely severe symptoms of anxiety/depression. This is an important area for future work to be conducted determine if these patients may benefit from additional support and psychosocial intervention.

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There are some limitations to this work. The study only examined current pain in a small sample recruited from three clinics in New South Wales, Australia. It will be important to understand the prevalence of chronic pain amongst a larger representative sample.

Understanding the implications of current pain on treatment is also an important area for further studies. Another limitation to be mindful of is that no objective assessments of substance use or reported pain were conducted to confirm self-reported findings. We did not have collateral data, such as functional data, available to confirm this subjective measure. However, more generally, self-report is generally accepted as reliable and valid in this population in a research context (23), and pain is typically accepted to be a subjective experience. Finally, the sample was a convenience sample, rather than being randomly selected. The main characteristics of the sample indicate there are no differences on gender, age or distribution of pharmacotherapy treatment types compared with the national sample, suggesting that the sampling strategy may not have overly biased the sample (11).

This work also has a number of strengths. Validated tools for measuring pain, depression, substance dependence and general health were used. Also, this sample included both methadone and buprenorphine patients who were recruited from a range of treatment settings, increasing the generalisability of the results. Finally, this work adds to the limited number of studies investigating pain prevalence in OST samples, building on the international literature on this important and under-researched topic. The finding that pain prevalence was lower than in previous studies suggests that further work may be important to understand what factors contribute to this finding. Some of the difference may be explained by the inconsistent methods of pain measurement employed across OST samples reported in the literature. Use of a consistent validated tool may assist in performing comparisons between samples and within samples over time. We can only speculate that some characteristics of the treatment setting such as universal healthcare and low cost access to substance dependence treatment may improve the health of OST patients more generally. This would be important to confirm with larger studies in international settings.

In conclusion, the high prevalence of severe mental health symptoms amongst this sample of opioid-dependent people with current pain suggests this is an important area for future work to determine if targeted screening for pain and other comorbidities may be warranted. The finding that current pain was not associated with increased illicit opioid use or other aberrant

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medication-related behaviors in this in-treatment sample reminds us that it should not be assumed that those in opioid-treatment will misuse medications in response to pain.

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