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Research paper

Depression and anxiety among chronic pain patients receiving prescription opioids and medical marijuana

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ABSTRACT

Background: High rates of depression and anxiety have been consistently reported among patients suffering from chronic pain. Prescription opioids are one of the most common modalities for pharmacological treatment of pain, however in recent years medical marijuana(MM) has been increasingly used for pain control in the US and in several countries worldwide. The aim of this study was to compare levels of depression and anxiety among pain patients receiving prescription opioids and MM.

Methods: Participants were patients suffering from chronic pain treated with prescription opioids (OP,N = 474), MM (N = 329) or both (OPMM,N = 77). Depression and anxiety were assessed using the depression module of the Patient Health Questionnaire (PHQ-9) and the Generalized Anxiety Disorder scale (GAD-7).

Results: Prevalence of depression among patients in the OP, MM and OPMM groups was 57.1%, 22.3% and 51.4%, respectively and rates of anxiety were 48.4%, 21.5% and 38.7%, respectively. After controlling for confounders, patients in the OP group were significantly more likely to screen positive for depression (Adjusted Odds Ratio(AOR) = 6.18;95%CI = 4.12–9.338) and anxiety(AOR = 4.12;CI = 3.84–5.71)) compared to those in the MM group. Individuals in the OPMM group were more prone for depression (AOR for depression = 3.34;CI = 1.52–7.34)) compared to those in the MM group.

Limitations: Cross-sectional study, restricting inference of causality.

Conclusions: Levels of depression and anxiety are higher among chronic pain patients receiving prescription opioids compared to those receiving MM. Findings should be taken into consideration when deciding on the most appropriate treatment modality for chronic pain, particularly among those at risk for depression and anxiety.

1. Introduction

Chronic pain has been reported to affect at least 8% of the population in developed countries annually (Andrew et al., 2014). The total healthcare cost associated with pain in the US has been estimated at $261 to $300 billion per year (Gaskin and Richard, 2012), with average annual costs of pain patients estimated to be three times higher than of individuals without chronic pain (Berger et al., 2004). Chronic pain has been associated with a significant decrease in daily activities, occupational productivity and quality of life (Breivik et al., 2006; Patel et al., 2012; Smith et al., 2007). In addition, individuals suffering from chronic pain have high rates of comorbid psychiatric disorders which may further reduce activity and quality of life, including drug and alcohol use disorders, mood and anxiety disorders (Demyttenaere et al., 2007; Feingold et al., 2016a; Gerrits et al., 2014, 2012).

The association between chronic pain, depression and anxiety has gained particular attention due to high rates of co-morbidity (Dersh et al., 2002). Up to 54% of pain patients have been reported to suffer from co-morbid depression, and up to 50% have been reported to suffer from anxiety, with particularly high rates of Generalized Anxiety Disorder (Gadermann et al., 2012), specific phobia and panic disorder (Banks and Kerns, 1996; Dersh et al., 2002; Knaster et al., 2012; McWilliams et al., 2003). The causal association between depression and anxiety and chronic pain is yet unclear, with findings supporting both an antecedent and consequent association (Magni et al., 1994;

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Polatin et al., 1993).

Prescription opioids are one of the most common modalities for the pharmacological treatment of pain, and have proven useful for the treatment of acute pain (Moore and McQuay, 1997; Shang and Gan, 2003) and pain related to cancer (Carr et al., 2004). In addition, these medications have been increasingly used for the treatment of chronic nonmalignant pain (Compton and Volkow, 2006). However, in the past two decades there is gradual awareness of public health risks associated with the increase in prescriptions to opioids (such as risks of diversion, overdose and addiction (Volkow and McLellan, 2016)) warranting the search for alternatives means for treatment of chronic pain. Medical marijuana (MM) has been used widely for pain control in the US and in several countries worldwide, becoming increasingly popular as a potential alternative to prescription opioids for the treatment of chronic pain (Hill, 2015; Jensen et al., 2015). However, due to great variability in the legal status of MM in different countries, data pertaining to the sociodemographic and clinical characteristics of chronic pain patients receiving MM compared to those receiving prescription opioids is scarce (Hall and Weier, 2015). Specifically, there is a lack of data regarding rates of co-occurring depression and anxiety among individuals receiving these two treatments. This may be important as the use of opioids and marijuana may in itself differentially affect levels of depression, anxiety and perceived pain.

The aim of the present study is to explore rates of depression and anxiety among individual receiving treatment for chronic pain, comparing individuals receiving prescription opioids and those receiving MM.

2. Materials and methods

2.1. Sample

Subjects for this study were recruited during a 6-month period in two large pain centers in Israel. Patients treated for chronic pain (i.e. pain lasting for more than three months (Elliott et al., 1999)) were approached for recruitment for the study. The response rate was 57%, encompassing a total of 890 participants. Patients participating in the study were not reimbursed for their participation and all subjects were required to sign an informed consent form prior to participation, which was then immediately detached from the questionnaire upon completion and indexed (in order to allow anonymous data collection and increase reliability of respondents' replies (Harrison, 1997)). This study was approved by the Institutional Review Board (IRB) committee at both medical centers.

3. Measures

3.1. Sociodemographic and clinical data

The following data was collected from each participant using self-administered questionnaires:

1. Socio-demographic data, including sex, age country of birth, type of residence (urban/rural), years of education, employment status, eligibility for disability allowance, marital status and number of children.
2. Medical history: participants were asked regarding lifetime diagnoses of common medical conditions including hypertension, liver disease, heart disease, ulcer or duodenum disease, migraine, herniated disc, arthritis and fibromyalgia.
3. History of substance use, including any twelve-month and lifetime use of the following substances: alcohol, cannabis, synthetic cannabinoids (‘Spice’, K2, etc.), MDMA, LSD, bath salts and heroin. This list was based on the most common substances used in Israel (Lev-Ran et al., 2014).
4. Pain indices – average level of pain (0–10) in the past month.

3.2. Psychiatric comorbidities

Co-occurring psychiatric disorders were screened for using the following tools:

1. The depression module of the Patient Health Questionnaire (PHQ-9): a nine items questionnaire based on DSM-IV criteria for major depressive disorder. Each item scored on a three-point scale (0 = not at all to 3 = nearly every day), with total scores of 5, 10, 15, and 20 representing cut-off points for mild, moderate, moderate-severe and severe depression, respectively. A score of 10 was used as a cut-off score indicating "positive" for screening of clinical depression (Kroenke et al., 2001). Sensitivity and specificity of the PHQ-9 have been reported to be 75% and 90%, respectively (Spitzer et al., 1999).
2. Generalized anxiety disorder scale (GAD-7): a 7-item measure based on DSM-IV criteria for GAD (Spitzer et al., 1999). Each item is rated on a 0–3 scale relating to the frequency of anxiety symptoms over the last two weeks (0 = ‘not at all’ to 3 = ‘nearly every day’ (Lowe et al., 2008)). Total scores of 5, 10, and 15 represent mild, moderate, and severe levels of anxiety. We used a score of 10 as the cut-off score indicating "positive" screening of GAD (Lowe et al., 2008). Sensitivity and specificity of the GAD-7 are 89% and 82%, respectively. Though GAD-7 was designed as a screening tool for Generalized Anxiety Disorder, it is regarded a reliable self-report measure of anxiety in the general population (Lowe et al., 2008).

3.3. Statistical analysis

In order to establish differences between levels of anxiety and depression among subjects receiving prescription opioids and those receiving MM, we categorized subjects into those receiving opioids exclusively (OP group), those receiving MM exclusively (MM group) and those receiving both (OPMM group). Multinomial regression analyses were used to compare prevalence rates of categorical variables, with individuals in the MM group set as the reference group. Independent-sample *t*-tests (two-tailed) were applied for comparison of continuous variables. In order to specifically compare the odds of depression or anxiety among groups, we used multiple logistic regression analyses in which MM was the reference group. In order to control for possible confounding effect of sociodemographic and clinical factors which may account for differences in level of misuse (Fillingim et al., 2009), each analysis was conducted in two progressive models: the first included an unadjusted analysis and the second controlled for the following confounders: sociodemographic variables, medical history, history of substance use, average level of pain and amount of time using pain medication. Analyses were performed using SPSS software, 21st version.

4. Results

Among participants, 474 (59%) were treated with prescription opioids exclusively, 329 (41%) were treated with MM exclusively and 77 (8.6%) received both. The remaining 10 subjects, receiving neither prescription opioids nor MM were excluded from analyses in this study. The proportion of women was significantly higher in the OP group compared to the MM group ($p < 0.01$) group, as was the proportion of patients receiving a disability allowance ($p < 0.01$) (Table 1). Patients in the OP group were more likely to report lifetime use of alcohol and drugs compared to those in the MM group ($p < 0.0.5$ for both). The most common substances concurrently used (past 12 months) among patients in the OP group were alcohol (31.6%), cannabis (18.2%) and LSD (1.1%), whereas the most common among those in the MM group were alcohol (37.2%), MDMA (0.6%) and LSD (0.3%) (naturally all MM patients were cannabis users). No significant differences were found in rates of common medical conditions between the two groups. Patients