Medical Cannabis Use Is Associated With Decreased Opiate Medication Use in a Retrospective Cross-Sectional Survey of Patients With Chronic Pain

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Abstract: Opioids are commonly used to treat patients with chronic pain (CP), though there is little evidence that they are effective for long term CP treatment. Previous studies reported strong associations between passage of medical cannabis laws and decrease in opioid overdose statewide. Our aim was to examine whether using medical cannabis for CP changed individual patterns of opioid use. Using an online questionnaire, we conducted a cross-sectional retrospective survey of 244 medical cannabis patients with CP who patronized a medical cannabis dispensary in Michigan between November 2013 and February 2015. Data collected included demographic information, changes in opioid use, quality of life, medication classes used, and medication side effects before and after initiation of cannabis usage. Among study participants, medical cannabis use was associated with a 64% decrease in opioid use (n = 118), decreased number and side effects of medications, and an improved quality of life (45%). This study suggests that many CP patients are essentially substituting medical cannabis for opioids and other medications for CP treatment, and finding the benefit and side effect profile of cannabis to be greater than these other classes of medications. More research is needed to validate this finding.

Perspective: This article suggests that using medical cannabis for CP treatment may benefit some CP patients. The reported improvement in quality of life, better side effect profile, and decreased opioid use should be confirmed by rigorous, longitudinal studies that also assess how CP patients use medical cannabis for pain management.

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Key words: Medical cannabis, opioids, chronic pain, side effects.

Chronic pain (CP) is among the most common and expensive medical conditions, affecting >100 million Americans, and with total direct and indirect costs of up to $635 billion per year. Despite their high prevalence, treatment of CP conditions is difficult. Treatments for CP conditions often require incremental lifestyle changes (exercise, sleep hygiene, stress reduction) and repeated doctor visits to monitor changes, which is increasingly challenging in the current economic and medical climate. Furthermore, other potentially efficacious therapies (eg, cognitive behavioral therapy and complementary approaches) are not often covered by insurance. Finally, opioids—one of the most common medication used to treat CP—are ineffective for many types of CP, as well as being addictive and associated with significant morbidity and mortality. Indeed, opioids are the most common prescription drug implicated in overdose deaths, involved in up to 75% of overdoses, and estimated to be responsible for at least 17,000 deaths annually.
Because of problems with the current treatment of pain, many patients and some providers have begun to re-examine the potential role for cannabis or cannabinoids for treating CP. Because there are no synthetic cannabinoids approved for treatment of CP in the United States, the most available form of cannabinoids for most patients is cannabis purchased from dispensaries or illegally. Cannabis has been legal in parts of the United States since 1996 for treatment of multiple conditions, including CP. Randomized controlled trials have examined whether cannabis, cannabis extracts, or synthetic cannabinoids are efficacious in CP states, with a recent meta-analysis suggesting that there is moderate evidence that some types of CP states may be improved by use of cannabinoids. In contrast, there have been relatively few studies of the effectiveness of cannabinoids in real-life settings. A study out of the Netherlands suggested that 53% of registered cannabis users consumed cannabis for enhanced pain control although other studies have described uncertain efficacy for CP treatment. Interestingly, legalization of medical cannabis was associated with a mean 24.8% decrease in opioid overdose deaths in multiple states across the United States. Although suggestive that cannabis could act as a replacement or alternative for opioids, this finding was on an ecological level, so changes at an individual level could not be gauged.

In our current study, we surveyed medical cannabis cardholders in Michigan, who must receive a certification from a licensed physician that they have a condition deemed by the statute to justify cannabis use (eg, CP) to obtain their permit. We hypothesized that many cannabis users were using cannabis for CP reduction and as a substitute for opioids. We further hypothesized that we may find some evidence that cannabis was reported to be more effective for CP that is “centralized” in nature. By centralized in nature, we mean individuals in whom the central nervous system is playing a greater role in pain, which we have previously shown is associated with decreased responsiveness to opioids. This is plausible because meta-analyses that have examined the efficacy of cannabinoids in neuropathic and centralized pain states have suggested that these compounds are generally efficacious whereas there is far less evidence for efficacy in nociceptive pain states. Thus, we hypothesized that individuals with higher scores on the 2011 Survey Criteria for fibromyalgia—a continuous measure that can be used to diagnose fibromyalgia as well as to determine the degree of pain centralization in CP states would show better overall pain relief with cannabis compared with those using cannabis for CP with lower scores on this measure. If this were to be true, then this would provide very preliminary evidence that cannabis might be a more effective treatment of centralized or neuropathic pain states than opioids, a finding in line with recent meta-analyses of the effects of cannabis in randomized controlled trials in various pain conditions.

Methods

Survey distribution was carried out in collaboration with owners of a local medical cannabis dispensary in Ann Arbor, Michigan, who helped recruit registered medical cannabis patients (18 years of age and older) to take the survey through the Qualtrics (Provo, UT) online survey platform. Study participants were enrolled between November 2013 and February 2015. Participant anonymity was maintained.

The survey contained 46 questions, detailing the medical condition(s) for which cannabis was used, method/frequency of cannabis use, changes in noncannabis medication use, changes in medication side effects, quality of life changes since starting cannabis use, and demographic information. As part of the survey, all participants completed the 2011 Fibromyalgia Survey Criteria (FM score), which gives a score from 0 to 31, with 31 indicating the most severe FM pain. This value indicates a participant’s FM score at the time of the survey, rather than their FM score before initiation of cannabis use. Survey questions of interest are shown in Table 1.

Statistics

The study population was examined using descriptive statistics. To ensure that no important information was missed by limiting analyses to fully completed questionnaires, sensitivity analyses were performed on the entire set of questionnaires, questionnaires that were ≥60% complete, ≥80% complete, and those that were fully completed (Table 2). There were very little differences between the outcomes, so analysis was limited to questionnaires that were fully completed. FM scores of participants were stratified into quartiles to examine whether degree of pain centralization was associated with outcomes of interest. Relationships between FM score quartile, opioid use change, quality of life change, when the study participant began using cannabis, and medication side effects were examined using Pearson correlation test. Student t-tests were used to examine whether cannabis use affected the number of medication classes (eg, opioids, nonsteroidal anti-inflammatory drugs, selective serotonin uptake inhibitor, disease modifying antirheumatic drugs, etc) taken, medication side effects, and paired t-tests were used to evaluate changes in these variables before and after initiation of cannabis use. Analysis of variance tests were used to examine whether changes in quality of life or opioid use were associated with FM score.

All analyses were carried out in R Studio version 0.98.1103 (R-Tools Technology Inc, Richmond Hill, Ontario, Canada).

Ethics Statement

This study was exempted from institutional review board oversight under protocol HUM00079724 at the University of Michigan. Participants freely consented to participate in the study, and were able to drop out at any time.
Results

Of the 374 participants in the study, 244 of the participants used cannabis to treat CP. Sensitivity analyses showed that exclusion of incomplete questionnaires did not have a significant effect on outcomes (Table 2), so only the complete questionnaires of participants with CP were used (n = 185).

Table 2. Sensitivity Analysis of Outcomes of Interest

<table>
<thead>
<tr>
<th>Outcome of Interest</th>
<th>Entire Set of Questionnaires (N = 244)</th>
<th>Questionnaires That Were ≥60% Completed (N = 192)</th>
<th>Questionnaires That Were ≥80% Completed (N = 186)</th>
<th>Questionnaires That Were Fully Completed (N = 185)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>FM score</td>
<td>9.23 (5.52)</td>
<td>9.28 (5.54)</td>
<td>9.15 (5.40)</td>
<td>9.16 (5.42)</td>
</tr>
<tr>
<td>Opioid use change</td>
<td>−63% (46%)</td>
<td>−63% (47%)</td>
<td>−64% (44%)</td>
<td>−64% (45%)</td>
</tr>
<tr>
<td>Degree to which side effects of medication affect daily function (before using medical cannabis); scale from 1 to 10</td>
<td>6.44 (2.91)</td>
<td>6.42 (2.91)</td>
<td>6.46 (2.89)</td>
<td>6.51 (2.88)</td>
</tr>
<tr>
<td>Degree to which side effects of medication affect daily function (after using medical cannabis); scale from 1 to 10</td>
<td>2.77 (2.35)</td>
<td>2.78 (2.36)</td>
<td>2.78 (2.38)</td>
<td>2.79 (2.39)</td>
</tr>
<tr>
<td>Number of medication classes used (before cannabis use)</td>
<td>2.35 (1.43)</td>
<td>2.34 (1.44)</td>
<td>2.36 (1.44)</td>
<td>2.38 (1.44)</td>
</tr>
<tr>
<td>Number of medication classes used (after cannabis use)</td>
<td>1.82 (.94)</td>
<td>1.84 (.95)</td>
<td>1.83 (.95)</td>
<td>1.81 (.95)</td>
</tr>
<tr>
<td>Quality of life change</td>
<td>45% (28%)</td>
<td>45% (28%)</td>
<td>45% (29%)</td>
<td>45% (29%)</td>
</tr>
</tbody>
</table>

NOTE. All quantities reported as mean (SD).

*Only fully completed questionnaires were used for final analyses.
Demographic information is summarized in Table 3. Of note, most participants (78.9%) smoked cannabis daily. Outcomes (opioid use change, quality of life change, number of medications, and medication side effects) in the total CP population and in FM score quartiles are summarized in Table 4.

**Effects of Cannabis on Opioid Use**

The mean change in self-reported opioid use among all respondents answering this question was −64%. Interestingly, in contrast to our hypothesis, the reduction of opioid use was the least drastic in the highest FM score quartile (−48%), which was significantly different from the lowest FM score quartile (−79%, P = .03) but not the second and third (−74% and −63%, P = .14 and .59, respectively).

**Effects of Cannabis on Number of Medication Classes Used and Side Effects of Medications**

The number of medication classes used after initiation of cannabis use was (1 + reported number) to account for cannabis use. Medications used before and after initiation of cannabis use are reported in Table 5. Although we focus in this article on opioid dosage reductions because this has become a major public health problem in the United States, there were comparable reductions in self-reported usage of many other classes of analgesic drugs. The mean number of medications classes used decreased significantly in all respondents before and after cannabis use (2.38 vs 1.81, respectively, P < .001).

Although we did not find our hypothesized findings that individuals with more centralized pain (eg, with a more fibromyalgia-like phenotype) reported increased effectiveness of cannabis, we did find that the degree of pain centralization predicted differential medication usage before and after cannabis use. Participants in the fourth FM score quartile used a significantly greater number of medication classes than those in the first, second, and third quartiles before initiation of cannabis use (P < .001, P < .001, P = .004, respectively). After initiation of cannabis use, participants in the fourth FM score quartile continued to use a significantly greater number of medication classes compared with those in the other quartiles (P < .001, P < .001, P = .068 in the first, second, and third quartiles, respectively). Side effects of medication on everyday functioning decreased substantially after cannabis use (6.51 vs 2.79, P < .001). There were no differences in the change in medication side effects among FM score quartiles (P = .86).

**Discussion**

Our primary study hypothesis that patients would self-report that they derived more pain relief from cannabis if they had more centralized pain was not supported. In fact, patients with lower pain centralization levels noted the best improvements in quality of life, as well as the largest reductions in opioid usage. However, this study did yield several significant findings. Overall, since the initiation of medical cannabis use, CP patients reported significant decreases in medication side effects that affected their daily functioning (including opioids), decreases in total number of medications being taken, and improvements in quality of life. Reported reduction in opioid use and decreased medication side effects were significantly correlated (r = .37, P = .0002), indicating a potential health benefit of replacing opioids with cannabis. This "opioid-sparing" effect is consistent with the ecological study by Bachhuber et al.² and hints to potential synergistic effects between cannabis and opioids for reduction of severe CP. Indeed, a recent study in Australia reported that people with CP had better pain reduction when they combined opioids and cannabis.⁵

**Limitations**

Although suggestive, the cross-sectional study design limits inference from our data, because our outcomes of interest (changes in quality of life, opioid use, side effects of medication, and number of medications) were measured with potentially unreliable recall data. Indeed, some study participants had been...
Table 4. Outcomes of Interest in the Study Population

<table>
<thead>
<tr>
<th>OUTCOME OF INTEREST</th>
<th>FM SCORE</th>
<th>QC 1</th>
<th>QC 2</th>
<th>QC 3</th>
<th>QC 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>FM score</td>
<td>9.16 (5.42)</td>
<td>3.61 (2.71)</td>
<td>7.12 (0.74)</td>
<td>10.40 (1.22)</td>
<td>16.95 (3.70)</td>
</tr>
<tr>
<td>Opioid use change</td>
<td>-64% (45%)</td>
<td>-79% (32%)</td>
<td>-74% (40%)</td>
<td>-63% (39%)</td>
<td>-48% (54%)</td>
</tr>
<tr>
<td>Degree to which side effects of medication affect daily function before using medical cannabis; scale from 1 (no effect) to 10 (significant effect)</td>
<td>6.51 (2.88)</td>
<td>5.89 (3.29)</td>
<td>5.7 (3.16)</td>
<td>7.06 (2.39)</td>
<td>7.22 (2.45)</td>
</tr>
<tr>
<td>Degree to which side effects of medication affect daily function after using medical cannabis; scale from 1 (no effect) to 10 (significant effect)</td>
<td>2.79 (2.39)</td>
<td>1.92 (1.96)</td>
<td>1.70 (1.29)</td>
<td>3.60 (2.76)</td>
<td>3.72 (2.46)</td>
</tr>
</tbody>
</table>

Table 5. Medication Classes Used Before and After Initiation of Cannabis Among the Study Population

<table>
<thead>
<tr>
<th>MEDICATION TYPE</th>
<th>USE BEFORE INITIATION OF CANNABIS, N/N (%)</th>
<th>USE AFTER INITIATION OF CANNABIS, N/N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opioids</td>
<td>119/184 (65)</td>
<td>33/184 (18)</td>
</tr>
<tr>
<td>Nonsteroidal anti-inflammatory</td>
<td>115/184 (62)</td>
<td>38/184 (21)</td>
</tr>
<tr>
<td>Disease-modifying antihypertensive drugs</td>
<td>15/184 (8)</td>
<td>3/184 (2)</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>72/184 (39)</td>
<td>25/184 (14)</td>
</tr>
<tr>
<td>Serotonin-norepinephrine</td>
<td>13/184 (7)</td>
<td>3/184 (2)</td>
</tr>
<tr>
<td>Selective serotonin inhibitors</td>
<td>34/184 (18)</td>
<td>3/184 (2)</td>
</tr>
<tr>
<td>Other</td>
<td>69/184 (38)</td>
<td>40/184 (22)</td>
</tr>
</tbody>
</table>

NOTE. FM score and quartiles for change in opioid use, quality of life, side effects of medications before and after cannabis use, and number of medication classes used before and after cannabis are presented. All quantities reported as mean (SD).
Although we caution against using this study to change clinical practice toward cannabis, this study provides intriguing hints of the value of cannabis, as an effective pain medication and as an effective agent against opioid overuse and overdose.

Acknowledgments
We thank Mark Passerini and Keith Lambert at Om of Medicine for their help on this project, and the Om of Medicine staff for their help in administering the survey.

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