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

Kevin F. Boehnke,* Evangelos Litinas,† and Daniel J. Clauw‡,§

*Department of Environmental Health Sciences, School of Public Health, University of Michigan, Ann Arbor, Michigan.
†Om of Medicine, Ann Arbor, Michigan.
‡Departments of Anesthesiology, Medicine (Rheumatology), and Psychiatry, Medical School, University of Michigan, Ann Arbor, Michigan.
§Chronic Pain and Fatigue Research Center, Medical School, University of Michigan, Ann Arbor, Michigan.

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.***

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.[8] 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.[14] 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.[1] 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.[10]

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Mr. Boehnke reports no conflicts of interest.

Address reprint requests to Daniel J. Clauw, MD, University of Michigan, 24 Frank Lloyd Wright Dr, PO Box 385, Ann Arbor, MI 48106. E-mail: dclauw@med.umich.edu

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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.[12] 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.[15] 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[7] although other studies have described uncertain efficacy for CP treatment.[6] Interestingly, legalization of medical cannabis was associated with a mean 24.8% decrease in opioid overdose deaths in multiple states across the United States.[2] 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.[3,4,9] 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,[13,15] whereas there is far less evidence for efficacy in nociceptive pain states.[16] 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[13]—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.[13,15]

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.[16] 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.

Table 1. Survey Questions Regarding Outcomes and Exposures of Interest

Survey Question	Answer Options
In a typical week, how often do you use cannabis?	• Less than once per week • One time • 2 to 3 times • 4 to 6 times • Daily
On a day that you do use cannabis, how often do you use it?	• Less than once • 1 to 2 times • 3 to 4 times • More than 5 times
When did you start using cannabis for medical purposes? Please give your answer in years.	Descriptive, ranges from 0 to 50 y
What classes of drugs were you using (check all that apply) before you started using cannabis? (Choose all that apply)	• Opioids (such as Vicodin*) • NSAIDs (such as aspirin) • Disease-modifying antirheumatic drugs • Antidepressants • Serotonin–norepinephrine reuptake inhibitors • Selective serotonin reuptake inhibitors • Other
On a scale of 1 to 10 (with 1 being not at all and 10 being significantly) how much did the side effects of the medications you took before using cannabis affect your ability to do the things you needed to accomplish each day?	1 through 10
On a scale of 1 to 10 (with 1 being not at all and 10 being significantly) how much do the side effects of the medications you take in combination with cannabis affect your ability to do the things you needed to accomplish each day?	1 through 10
How has your opioid prescription drug use changed since you started using cannabis? Increase or decrease (%). If your opioid use has increased by 30%, please write +30%. If your opioid use has decreased by 30%, please write in −30%.	−100% through +100%
Are you taking any of the following drugs or drug classes in combination with cannabis? (Choose all that apply)	• Opioids (such as Vicodin*) • NSAIDs (such as aspirin) • Disease-modifying antirheumatic drugs • Antidepressants • Serotonin–norepinephrine reuptake inhibitors • Selective serotonin reuptake inhibitors • Other

Abbreviation: NSAID, nonsteroidal anti-inflammatory drug.
*Vicodin manufactured by AbbVie Inc (North Chicago, IL).

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

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

NOTE. All quantities reported as mean (SD).
*Only fully completed questionnaires were used for final analyses.

Table 3. Demographic Characteristics of the Study Population (n = 185)

Variable	Value
Sex	
Male	118 (64)
Female	65 (35)
Refuse to answer	2 (1)
Age	
18 to 25	32 (17)
26 to 35	40 (22)
36 to 45	32 (17)
46 to 55	25 (14)
56 to 65	46 (25)
66 to 75	9 (5)
Refuse to answer	1 (.5)
Weekly cannabis use	
<1 Time	1 (.5)
2 to 3 times	16 (9)
4 to 6 times	22 (12)
Daily	146 (79)
Daily cannabis use	
1 Time	22 (12)
2 Times	47 (25)
3 to 4 times	77 (42)
≥5 Times	38 (20)
Refuse to answer	1 (.5)
Opioid use before cannabis use	
Yes	119 (64)*
No	66 (36)
CP status	
Yes	185 (100)

NOTE. Data are presented as n (%).
*One participant chose not to respond to the question about change in opioid use.

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 usage. 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

Outcome of Interest	CP (N = 185)	FM Score Quartile 1 (N = 56)	FM Score Quartile 2 (N = 42)	FM Score Quartile 3 (N = 43)	FM Score Quartile 4 (N = 44)
FM score	9.16 (5.42) n = 185	3.61 (1.27) n = 56	7.12 (0.74) n = 42	10.40 (1.22) n = 43	16.95 (3.70) n = 44
Opioid use change (−100% to +100%)	−64% (45%) n = 118	−79% (32%) n = 28	−74% (40%) n = 22	−63% (39%) n = 30	−48% (54%) n = 38
Degree to which side effects of medication affect daily function before using medical cannabis; scale from 1 (no effect) to 10 (significant effect)	6.51 (2.88) n = 136	5.89 (3.29) n = 38	5.7 (3.16) n = 27	7.06 (2.39) n = 35	7.22 (2.45) n = 36
Degree to which side effects of medication affect daily function after using medical cannabis; scale from 1 (no effect) to 10 (significant effect)	2.79 (2.39) n = 136	1.92 (1.96) n = 38	1.70 (1.29) n = 27	3.60 (2.76) n = 35	3.72 (2.46) n = 36
Change in medication side effects after initiation of cannabis	−3.72 (3.42) n = 136	−3.97 (3.72) n = 38	−4.00 (3.25) n = 27	−3.46 (3.31) n = 35	−3.50 (3.43) n = 36
Number of medication classes used (before cannabis use)	2.38 (1.44) n = 184	1.96 (1.36) n = 56	1.88 (1.10) n = 41	2.40 (1.35) n = 43	3.3 (1.46) n = 44
Number of medication classes used (after cannabis use)	1.81 (.95) n = 184	1.46 (.69) n = 56	1.54 (.67) n = 41	1.95 (1.11) n = 43	2.39 (.99) n = 44
Change in quality of life (−100% to +100%)	+45% (29%) n = 180	+54% (31%) n = 54	+43% (26%) n = 41	+44% (28%) n = 42	+38% (27%) n = 43

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).

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

Medication Type	Use Before Initiation of Cannabis, n/N (%)	Use After Initiation of Cannabis, n/N (%)
Opioids	119/184 (65)	33/184 (18)
Nonsteroidal anti-inflammatory drugs	115/184 (62)	38/184 (21)
Disease-modifying antirheumatic drugs	15/184 (8)	3/184 (2)
Antidepressants	72/184 (39)	25/184 (14)
Serotonin–norepinephrine reuptake inhibitors	13/184 (7)	3/184 (2)
Selective serotonin reuptake inhibitors	34/184 (18)	8/184 (4)
Other	69/184 (38)	40/184 (22)

NOTE. Study participants reported using fewer medication classes of all categories after initiation of cannabis use.

using cannabis for medical purposes for quite some time (median of 4 years). FM scores were measured at the time of the survey, so we were unable to know participant's baseline FM score before they started using cannabis, potentially biasing the data. Furthermore, our results may not be representative of the general population, because we only surveyed patrons of a medical cannabis dispensary. Finally, with the recent attention to opioid overuse and overdose, we considered the possibility that physicians would reduce the number of opioid prescriptions, which could have happened concurrently with our study. This could provide an explanation for the drastic decrease in the use of opioids that we report. However, the Michigan Department of Community Health and the Michigan Automated Prescription System showed consistent increases in the number opioid prescriptions written from 2007 to 2014 (7.7 million in 2007 to 9.7 million in 2014) and in the number of opioid units prescribed from 2011 to 2014 (over 620 million units total in 2011 to almost 677 million in 2014).[11,17] Although we do not know if the statewide trends apply to our study, our observed decreased opioid use is not consistent with these trends, suggesting that it may be due to other factors (including the use of cannabis).

Future Directions and Conclusions

Future studies can address these issues by using longitudinal study designs that recruit participants naive to cannabis and measure their pain levels before and after using cannabis. This would make the results more robust by taking into account temporality, and resolve issues of selection bias in our current study. We plan to continue recruiting participants for this study to validate the robustness of our results in a larger population. Because cannabis is a schedule I drug, much of the literature surrounding its efficacy as medication is anecdotal and/or not peer-reviewed.

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.

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