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Clinical Studies

Cannabis use is associated with decreased opioid prescription fulfillment following single level anterior cervical discectomy and fusion (ACDF)

Jacob Silver, MD[a,*], Colin Pavano, MD[a], Nicholas Bellas, MD[a], Cory Hewitt, MD[a], Barrett Torre, MD[a], Mathew Solomito, PhD[b], Regina Kostyun, MSEd[b], Sean Esmende, MD[b]

[a] UConn Health Center, University of Connecticut School of Medicine, 263 Farmington Ave, Farmington, CT 06030, United States
[b] Hartford Hospital, Bone and Joint Institute, Hartford, CT

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ABSTRACT

Background: Recently, there has been increasing legalization of marijuana within the United States, however data are mixed with respect to its efficacy in treating acute pain. Our goal was to identify a difference in opioid utilization in patients with known cannabis use before anterior cervical discectomy and fusion (ACDF) compared with those that report no cannabis use.

Methods: This study was a retrospective case-control design using PearlDiver. Patients who underwent a single level ACDF between January 2010 and October 2020, were included. Patients were placed in the study group if they had a previous diagnosis of cannabis use, dependence, or abuse. Patients were excluded if they were under the age of 18 or if they had filled an opioid prescription within 3 months of their procedure. A control group was then created using a propensity score match on age, gender, and Charleston comorbidity index (CCI), and had no diagnosis of cannabis use. The primary outcome was the number of morphine milliequivalents (MME) dispensed per prescription following surgery.

Results: A total of 1,339 patients were included in each group. The number of patients filling prescriptions was lower in the cannabis group than in the control group at 3 days postoperatively ($p<.001$). The average total MME per day as prescribed was lower in the cannabis group than the control group at 60 days post-op (48.5 vs. 59.4, respectively; $p=.018$).

Conclusions: Patients who had a previous diagnosis of cannabis use, dependence or abuse filled fewer opioid prescriptions postoperatively (at 3 days postoperatively) and required lower doses (reduced average daily MME, at 60 days postoperatively) when compared with the control group.

Introduction

Over the past decade the legal landscape concerning cannabis use in the United States has shifted in favor of allowing marijuana usage for both medical and recreational use [1,2]. This shift has led to a significant increase in research related to the medical utility of cannabis [3–6]. There is growing evidence to suggest that cannabis use may positively impact opioid consumption [7,8]. In vitro data have suggested that cannabis may have a synergistic effect with opioids that allows for similar analgesic effects with lower opioid doses [9]. Despite the growing body of literature concerning the medical ramifications of cannabis use there are only a handful of studies that explore its use in an orthopedic population and the results of these studies are in some cases contradictory [10,11]. Studies in favor of cannabis use have demonstrated that recreational marijuana users reported less pain, better mobility, and shorter lengths of stay following lumbar spine procedures [11–13]. However, recent studies have also indicated that marijuana users tended to require more opioid pain medication, have greater postoperative pain, poor sleep quality, and greater complication rates [14,15].

Anterior cervical discectomy and fusion (ACDF) is a common spine surgery often necessitating opioid pain management for patient comfort postoperatively. Given the prevalence of the ACDF procedure in the United States and the continued need for opioid stewardship, this population provides an opportunity to determine if cannabis may serve

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* Corresponding author. UConn Health Center, University of Connecticut School of Medicine, 263 Farmington Ave, Farmington, CT 06030, USA. Tel.: (585) 738-0177.

E-mail address: Jsilver@uchc.edu (J. Silver).

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as an alternative/adjunct for pain control. This study utilized a large claims database to determine whether preoperative cannabis use in patients undergoing elective ACDF procedures was associated with lower utilization of opioid medication.

Methods

This was a retrospective case-control study using PearlDiver (PearlDiver Inc.), a proprietary web-based research platform that contains adjudicated medical claims data from Commercial, Medicare, Medicaid, Government, and cash payers. At the time this study was performed, there were over 91 million records from January 2010 through October 2020. The institutional review board at our institution deemed this study exempt.

Inclusion criteria

Patient records were queried to identify those who underwent a single level cervical fusion using current procedural terminology (CPT) code 22551. Patient records were excluded if the patients were under the age of 18 years old, were not continuously enrolled in the dataset for a minimum of 90 days before and 90 days following their surgical procedure, or had filled an opioid prescription within 3 months of their ACDF. Patients were placed into the study group if they previously used cannabis before their surgery. Cannabis use was determined using International Classification of Diseases, Ninth and Tenth Revisions (ICD-9 and ICD-10) codes for cannabis use, abuse, or dependence (ICD-9 304.30 and 305.20, ICD-10 F12.10, F12.20, and F12.90). The control group was created using a 1:1 propensity score matching on age, sex, and Charlson comorbidity index (CCI), with a caliper of 0.2. The CCI is a scoring system initially developed in 1987 as a means of predicting risk of death within 1 year of a hospital encounter. It takes into account a total of 19 health-related conditions [16].

Outcomes

The primary outcome was opioid prescription fulfillment determined from the Uniform System of Classification (USC) drug database within PearlDiver (USC-02211, USC-02212, USC-02214, USC-02221, USC-2222, and USC-02232). The primary outcome variables were the number of patients that filled their opioid prescription, and how many patients filled additional opioid prescriptions within 90 days of their procedure. To provide an additional level of detail opioid prescriptions were assessed from 0 to 3 days postindex procedures, and data were stratified at 3 days postoperative, 4 to 30 days postindex procedure and data for this level were stratified at 30 days postoperative, 31 to 60 days postindex procedures and stratified as 60 days postoperative, and finally between postoperative days 61 and 90 and these data were stratified as 90 days postoperative. Additional variables extracted from the database included: average opioid dose per prescription as measured by morphine milliequivalents (MME) and average daily MME per prescription. The data provided from the database details both the total MME per prescription as well as total prescribed daily MME; from these data points it would have been possible to determine the total number of days that the prescription was given. However, given the limitation that these data were based on filled prescriptions it was impossible to determine for how long a patient actually used the medication or what quantity they used.

Statistics

All statistical analyses were performed using R studio software version 3.6.1 embedded within the PearlDiver application. General descriptive statistics were used to describe all parameters of interest, continuous data were presented as means and standard deviations, discrete data were presented as medians and ranges, and binary data were presented as the percentage of the total study population. Differences between groups were assessed using *T* tests assuming unequal variances or a Mann—Whitney *U* test based on the distribution of the data were used to compare continuous variables while binary and categorical data were assessed using a chi-squared contingency test. A p value of .05 was considered to be statically significant. Repeated independent chi-squared tests were performed for each time point of interest in regards to number of prescriptions filled. To account for the repeated testing an adjusted p value, as determined using a Bonferroni correction, of less than .0125 was considered statistically significant. It is also important to note that when the cell values were below 5 a Fisher exact test was used in place of the chi-square testing.

Results

A total of 2,678 patients were analyzed as part of this study, 1,339 patients were included in the cannabis use group (Table 1). No significant demographic differences were observed between groups (Table 1).

Over 7% of patients in the control group filled their initial opioid prescription compared with 2.7% in the cannabis use group within 3 days of surgery (p<.001, Table 2). There were no differences for patients filling their initial prescriptions at 30, and 60 days postindex procedure (p=.125 and p=.205, respectively). No patients within the cannabis group filled their initial prescriptions at 90 days postindex procedure. There was a significant difference in daily MME dose prescribed for those patients filling a prescription 60 days postsurgery between groups (p=.018, Table 2).

About 3.1% of the control group and 1.8% of the cannabis group filled additional opioid prescriptions, when looking at the total number of patients. However, when looking at only those patients that filled an initial prescription it was noted that the cannabis group did have a higher rate of additional prescriptions at 30 days postindex procedure, where nearly 34% of the cannabis group and 24% of the control group filled additional prescriptions. However, this difference was not statistically significant (p=.181) (Table 3). Again, there were no differences in number of prescriptions filled at both 60 and 90 days postindex procedure (p=.453 and p=.859, respectively). There was no statistical difference between study groups in overall MME or daily MME doses (Table 3).

Discussion

The purpose of this study was to determine if cannabis use in patients undergoing elective ACDF surgery was associated with postoperative opioid prescription fulfillment. The results demonstrated that patients with a history of cannabis use, abuse, or dependency filled fewer prescriptions for opioid pain medication than the control group.

Table 1
Demographic comparison between the cannabis and control groups

	Cannabis group	Control group	p value
N	1,339	1,339	
Age range			
18–19	<11	<11	.055
20–29	52 (3.9%)	<11	
30–39	202 (15.1%)	165 (12.3%)	
40–49	385 (28.8%)	398 (29.7%)	
50–59	415 (31.0%)	474 (35.4%)	
60–69	209 (15.6%)	230 (17.2%)	
70–79	69 (5.2%)	<11	
>80	<11	<11	
Sex			
Male	526 (39.3%)	535 (40.0%)	.722
Female	813 (60.7%)	804 (60.0%)	

Table 2
Comparison of the initial opioid prescriptions between the cannabis and control groups

	3 days post-op	30 days post-op	60 days post-op	90 days post-op
Number of patients filling prescriptions (n)				
Control group	100 (7.5%)	22 (1.6%)	3 (0.2%)	6 (0.4%)
Cannabis group	36 (2.7%)	13 (0.9%)	7 (0.5%)	0 (0%)
p value	**<.001**[a]	.125	.205	–
Average total opioid dose per prescription (MME)				
Control group	487.2 (90–2520)	465.6 (90–2520)	464.1 (90–2520)	458.7 (90–2520)
Cannabis group	373.4 (140–1350)	411.4 (160–1800)	417.3 (207–1800)	–
p value	.065	.123	.148	–
Average total daily opioid dose prescribed (MME)				
Control group	62.4 (26–180)	59.7 (18–180)	59.4 (18–180)	59.5 (18–180)
Cannabis group	52.2 (20–90)	51.5 (23–108)	48.5 (14–108)	–
p value	.088	.091	**.018**[a]	

Data presented as mean (range).
[a] Bold value significance: p<.001.

Table 3
Comparison of the patients in each study group requiring an additional prescription

	30 days post-op	60 days post-op	90 days post-op
Number of patients filling prescriptions (n)			
Control group	32 (24.4%)	6 (4.5%)	4 (3.1%)
Cannabis group	19 (33.9%)	4 (7.1%)	2 (3.5%)33
p value	.181	.453	.859
Average total opioid dose per prescription (MME)			
Control group	484.5 (90–1200)	430 (225–1200)	428 (216–1109)
Cannabis group	369 (180–640)	404 (150–1350)	450 (150–1350)
p value	.525	.794	.382
Average total daily opioid dose prescribed (MME)			
Control group	48 (30–96)	45 (15–96)	41.5 (15–96)
Cannabis group	46 (25–70)	45 (21–80)	46 (21–90)
p value	.738	.607	.421

Data presented as mean (range). Percentages based on number of patients filling the initial opioid prescription.

Fewer patients in the cannabis group filled their opioid prescriptions within 3 days postoperatively. While we only observed this to be statistically significant at one time point postoperatively, this is consistent with current literature indicating that cannabis users reported lower pain levels and required less opioid medication than nonusers [7,9]. It was also noted that cannabis users tended to fill considerably fewer prescriptions within the first 3 days postoperatively than the control group (7.5% compared with 2.7%, respectively).

Daily MME doses in the cannabis group were below 50 MME for prescriptions filled within 60 days postoperatively in the cannabis group whereas the control group was at the 60 MME level at the same time point (p=.018). The 50 MME threshold is important as studies have suggested that opioid doses above 50 MME per day are significantly associated with an increased risk of opioid related death and/or hospitalization [17]. This suggests that patients using cannabis may be at a reduced risk of opioid dependence than nonusers.

Further investigation is necessary to establish the potential benefits of cannabis use in this patient population. The efficacy of cannabis remains equivocal, with mixed results reported in the literature. A retrospective cohort study conducted by Liu et al. found that patients who reported marijuana use experienced higher levels of pain in the immediate postoperative period. Their study focused on the first 36 hours following surgery. It is possible that the impact of cannabis on opioid usage may be change depending on timing postoperatively, which could be a reason for observed variation in the literature.

In 2022, Razzouk et al. published a study indicating that patients with a history of cannabis use who underwent ACDF had a higher consumption of MME during the 6 to 12 months following the operation than those who did not use cannabis [18]. Although a similar trend was observed in the 0- to 6-month postoperative period, it did not reach statistical significance. These findings underscore the importance of examining the potential impact of cannabis on the postoperative period, as well as the limited data currently available and the necessity for further investigation.

This study was not without limitations, there were inherent limitations to the use of a large insurance claims database. One such limitation was data were based solely on billable codes, and thus may cause selection bias especially in the cannabis group where the accuracy of diagnosis codes surrounding cannabis use is questionable. Therefore, it is likely that cannabis use is underrepresented in this study. Additionally, the codes used were generic to cannabis and do not make a distinction between CBD products or THC products, which may have significantly different effects both toward general health and opioid need. Additionally, the database was designed to indicate if an opioid prescription filled, there was no information as to how much of the prescription was used if any after being filled, and thus may skew some of the data as the results were presented assuming that the prescriptions were used in full. Finally, in an effort to reduce as many confounding variables as possible very stringent definitions were used for both opioid prescription and patient inclusion. This was an intentional decision to produce most accurate estimates possible but the conservative approach used in this study may limit its generalizability to a larger patient population. Additionally, it should be noted that patients previously using opioid based medications were excluded from this study. However, we did not explicitly exclude patients with an ICD9/10 diagnosis code for opioid abuse/dependency as it was felt that by excluding opioid use this would remove active users of opioid medications, while those with the code for dependency may still carry a code that is no longer relevant in regards to this study.

It is worth mentioning that the legalization of marijuana in the United States has been constantly changing over time. From 2010 to 2020, the period covered by our database, 15 states implemented laws that partially or fully legalized marijuana. As the use and perception of marijuana continue to develop, our ability to gather precise data may

improve as patients become more forthcoming about their usage, have more access to both medical and recreational products, and receive better education on the advantages and risks of marijuana. These ongoing changes will inevitably affect the reliability of data collection in this field.

Conclusions

In summary, patients who were known to use cannabis filled fewer opioid prescriptions following ACDF procedures and were prescribed lower daily doses than the control group, suggesting that cannabis use may reduce opioid requirements in this population. However, there is a clear need for future studies to investigate the effect that cannabis use may have on postoperative pain control.

Declarations of Competing Interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] Ghosh TS, Van Dyke M, Maffey A, et al. Medical marijuana's public health lessons – implications for retail marijuana in Colorado. NEJM 2015;372:991–3.
[2] Center for Behavioral Health Statistics and Quality. Mental Health Indicators in the United States: Results From the 2015 National Survey on Drug Use and Health. HHS pub. no SMA 16-4984, NSDUH series H-51. Rockville, MD: Substance Abuse and Mental Health Services Administration; 2016. p. 16-4984.
[3] Deshpande A, Mailis-Gagnon A, Zoheiry N, Lakha SF. Efficacy and adverse effects of medical marijuana for chronic noncancer pain: systematic review of randomized controlled trials. Can Fam Phys 2015;61(8):e372–81.
[4] Volkow ND, Baler RD, Compton WM, et al. Adverse health effects of marijuana use. NEJM 2014;370:2219–27.
[5] Jouanjus E, Lapeyre-Mestre M, Micallef J. Cannabis use: signal of increasing risk of serious cardiovascular disorders. J Am Heart Assoc 2014;3(2):e000638.
[6] Moussouttas M. Cannabis use and cerebrovascular disease. Neurologist 2004;10(1):47–53.
[7] Liang D, Bao Y, Wallace M, Grant I, Shi Y. Medical cannabis legalization and opioid prescriptions: evidence on US Medicaid enrollees during 1993-2014. Addiction 2018;113(11):2060–70.
[8] Madden K, George A, Van Der Hoek NJ, Borim FM, Mammen G, Bhandari M. Cannabis for pain in orthopedics: a systematic review focusing on study methodology. Can J Surg 2019;62(6):369–80.
[9] Temple LM. Medical marijuana and pain management. Dis Mon 2016;62(9):346–52.
[10] Hickernell TR, Lakra A, Berg A, Cooper HJ, Geller JA, Shah RP. Should cannabinoids be added to multimodal pain regimens after total hip and knee arthroplasty? J Arthroplasty 2018;33(12):3637–41.
[11] Bhashyam AR, Heng M, Harris MB, Vrahas MS, Weaver MJ. Self-reported marijuana use is associated with increased use of prescription opioids following traumatic musculoskeletal injury. J Bone Joint Surg Am 2018;100(24):2095–102.
[12] Medina SH, Nadarajah V, Jauregui JJ, et al. Orthopaedic surgery patients who use recreational marijuana have less pre-operative pain. Int Orthop 2019;43(2):283–92.
[13] Liu CW, Bhatia A, Buzon-Tan A, et al. Weeding out the problem: the impact of preoperative cannabinoid use on pain in the perioperative period. Anesth Analg 2019;129(3):874–81.
[14] Chiu RG, Patel S, Siddiqui N, et al. Cannabis abuse and perioperative complications following inpatient spine surgery in the United States. Spine 2021;46(11):734–43.
[15] Jakoi AM, Kirchner GJ, Kerbel YE, et al. The effect of marijuana use on lumbar spinal fusion. Spine 2019;45(9):629–34.
[16] Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and valdiation. J Chronic Dis 1987;40(5):373–83.
[17] Nam YH, Bilker WB, DeMayo FJ, Neuman MD, Hennessy S. Incidence rates of and risk factors for opioid overdose in new users of prescription opioids among US Medicaid enrollees: a cohort study. Pharmacoepidemiol Drug Saf 2020;29(8):931–8.
[18] Razzouk J, Chung JH, Lindsey W, Ramos O, Cheng W, Danisa O. Preoperative cannabis use associated with an increased rate of reoperation and postoperative opioid use following anterior cervical decompression and fusion. Cureus 2022;14(11):e31285. doi:10.7759/cureus.31285.