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Friend or Foe: The Use of Cannabis as a Potential Analgesic in Postoperative Lumbar Spine Surgery

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ABSTRACT

Cannabis is a plant-based product which has been documented in medicinal usage dating back nearly 5000 years ago in 400 AD. With time, cannabis would come to become the most grown, cultivated, trafficked, and abused illicit drug worldwide. As a result, cannabis became a schedule 1 substance having no accepted medical use. In 1996, however, cannabis emerged in the medicinal scene when California became the first state to allow legal access to cannabis for medicinal purposes under the Compassionate Use Act. As of November 8, 2023, 24 states, two territories, and the District of Columbia all enacted laws to help regulate not only the use of marijuana medicinally but recreational use as well. A large proponent for the shift regarding the utilization of medicinal cannabis occurred as a direct result of the opioid abuse crisis which came to fruition in the late 1990s due to their outstanding ability to mitigate the human kryptonite; Pain. The goal of the present literature review is to better consolidate and critically think about the usage of cannabis perioperatively and its utility as a postoperative pain mitigator. More so, many current review articles, systematic reviews, and retrospective reviews suggest deleterious effects of the patient population undergoing lumbar spine surgery who also engage in cannabis usage. However, a lack of level I evidence continues to exist surrounding the clinical question of cannabis usage as a perioperative pain mitigator, leading to inconclusive recommendations regarding its utility. The present review aims to highlight the multitude of conflicting research and identify gaps in questions, which may lead to better utilization and recognition of cannabis as either a helpful or hurtful pain remedy.

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Overview

Cannabis, a plant, also commonly referred to as marijuana, contains chemical compounds that have been used for both medical and recreational purposes. Cannabis has two predominant biologically active molecules, THC

tetrahydrocannabinol, which is known to be the psychoactive component, whereas cannabidiol (CBD) is known for its therapeutic effects, such as analgesia. Cannabis has historically been inhaled but, in recent times with increasing legality, is now available as a medical grade liquid and pill.

In the United States, lumbar spine surgery is a commonly performed procedure due to the high incidence of degenerative lumbar spine conditions such as spinal stenosis or degenerative spondylolisthesis.[1] Patients undergoing surgery for degenerative lumbar spine conditions typically have high postoperative opioid use, especially given that many of these patients use opioids preoperatively and continue to do so long term postoperatively.[2] Considering the ongoing opioid crisis, the utility of cannabis as a postoperative pain mitigator in conjunction with other components of multimodal analgesia has not been thoroughly vetted in the literature. To date, no published randomized control trials have evaluated the use of cannabis in patients undergoing lumbar spine surgery, particularly regarding the efficacy of cannabis as an analgesic agent. The purpose of this review was to critically evaluate the current literature to determine whether the evidence supports or refutes the use of cannabis as a postoperative analgesia regimen modality.

Pain and Development of an Opioid Crisis

In 2013, Florence et al[3] published a landmark article to inform clinicians of the ongoing opioid crisis that had occurred secondary to increased narcotic prescriptions in the United States that occurred throughout the late 1990s. Using cost data from various sources including the Truven Health MarketScan Research Databases and the cost of fatal cases from Web-based Injury Statistics Query and Reporting System (WISQARS), Florence et al estimated the total economic burden of prescription opioid overdoses, abuse, and dependence to be $78.5 billion. Unfortunately, approximately one-third of this amount was attributed to an increase in healthcare and substance abuse treatment costs ($28.9 billion). Subsequently on October 26th, 2017, President Donald J. Trump declared the opioid crisis a public health emergency.[4] As of 2018, approximately two million people were documented to be diagnosed with opioid use disorder with nearly 48,000 deaths the year prior, in 2017, attributed to opioid-related abuse.[5,6]

It is important to understand the basic pain pathway through which opioids modulate pain. Physiologically, there are four natural opioid receptors (mu, kappa, delta, and opioid receptor like-1) that when stimulated will produce downstream effects such as analgesia. Opioids themselves may be endogenous (enkephalins, endorphins, and dynorphins) or nonendogenous. Nonendogenous opioids can be classified as either natural, semisynthetic, or synthetic. Semisynthetic opioids such as oxycodone are metabolized into two metabolically active metabolites that function as agonists of the mu receptor allowing them to achieve analgesia.

Given the painful nature of certain pathologies within the lumbar spine (i.e., diskogenic disease and spinal stenosis) and the surgical procedures meant to address them, semisynthetic opioid options such as oxycodone are commonly prescribed for postoperative pain control.[7] As healthcare providers, orthopaedic surgeons are the third highest prescribers of opioids, and thus, knowledge of the estimated cost burdens on the healthcare system and the consequence of unchecked opioid usage are vital.[8]

Cannabis—History, Epidemiology, and Pain Pathway

Cannabis was described initially in the US Pharmacopoeia of 1850 and was used medically during the 19th and early 20th centuries. Cannabis was then removed from the US Pharmacopoeia in 1942 and became a schedule 1 substance with no accepted medical use.[9] This was driven by the "anti-marijuana law" of 1937 where the US Federal government received political pressure from law enforcement agencies and the Department of the Treasury who feared the spread of marijuana usage from "Latin America."[10] Gradually, there was a thawing attitude regarding cannabis during the second half of the 1900s/20th century, and in 1996, California became the first state to allow legal access to cannabis for medicinal purposes under the Compassionate Use Act.

The decision to permit use of cannabis in medicinal pain amelioration stemmed from its purported neuroprotective effects in downstream pain pathways. The pathways are linked to effects of endocannabinoid on their receptors throughout the human body. Cannabinoid receptors 1 and 2 (CB-1 and CB-2) are G-protein–coupled receptors located within the central nervous system (CNS) and peripheral nervous system (PNS), respectively.[9] Peripheral analgesic effects of endocannabinoids occur through a neuronal mechanism mediated by the CB-1 receptors in the cell bodies of primary afferent neurons in the dorsal horn of the spinal cord. By activating CB-1 receptors, cannabinoids inhibit calcium release at the presynaptic membrane, which reduces nociceptive signaling.[11] CB-2 receptors are

found in immune cells within the central and peripheral nervous system and also contribute to the analgesic effects of cannabinoids.[11,12] CB-2 receptors when activated by cannabinoids stimulate release of cytokines which then cause indirect stimulation of mu-opioids receptors. Another postulated mechanism for the analgesic effects from cannabinoids is through CB-2 receptor-mediated effects of diminishing nerve growth factor (NGF)–induced mast cell degradation and neutrophil accumulation that otherwise lead to inflammatory hyperalgesia.[13]

Preclinical has demonstrated multiple pathways in which cannabis is able to provide pain control through activation of CB-1 and CB-2 receptors.[11-13] This has been further translated into clinical medicine, especially in the field of orthopaedics. In a placebo-controlled double-blind randomized trial, Alaia et al[14] demonstrated that cannabis naive patients who underwent arthroscopic rotator cuff repair had notable pain reduction postoperatively when using buccal cannabidiol. Despite this study and others like it, the therapeutic efficacy of cannabis for pain control remains elusive. Eisenberg et al[15] recognized that the ability to target a therapeutic efficacy for cannabis in pain control is incredibly challenging because many of the established randomized controlled trials evaluating cannabis usage as a pain mitigator vary tremendously in ratios of THC to CBD, routes of administration, and duration of treatment.

Previous literature has demonstrated that cannabinoids are effective and safe treatment for chronic neuropathic pain.[16] Whiting et al[17] in a landmark paper conducted a systematic review of randomized clinical trials of cannabinoid use for a variety of medical conditions including sleep disorders, chronic pain, and spasticity among many. They reported moderate quality evidence supporting cannabis use in chronic pain and spasticity. Low-quality evidence demonstrated an association of improved nausea and vomiting in chemotherapy patients who used cannabis and benefits to cannabis usage for patients with sleep disorders and Tourette syndrome. However, there are well-known short-term adverse effects of cannabis such as impaired short-term memory, impaired motor coordination, altered judgment, paranoia, or psychosis. Long-term or heavy use of cannabis has been related to addiction, cognitive impairment, chronic bronchitis, and increased risk of chronic psychosis-related health disorders such as schizophrenia. In addition, cannabis use has been associated with myocardial infarctions, stroke, and transient ischemic attacks.[9] Despite these temporary short-term adverse effects and relatively rare effects from chronic or heavy cannabis usage, cannabis overall has a relatively safe adverse effect profile and demonstrated promise in treatment of chronic neuropathic pain.[9,16] Given this known analgesic effect, it is reasonable to consider the role in postoperative pain control for lumbar spine surgery, however, to date, the role of cannabis for acute pain management postlumbar spine surgery is not well documented in current literature.[18]

Lumbar Spine Pathology and Surgery: Pain and Opioid Usage

Low back pain and lumbar spine pathology are commonly documented causes of pain and disability. Data from the Global Burden of Disease, Injuries, and Risk Factors Study between 1990 and 2017 demonstrated that low back pain was the leading cause of disability globally.[19] Patients with chronic back pain who have been on long-term opioid therapy preoperatively and subsequently undergo a lumbar surgical procedure are at higher risk of complications and poor outcomes. Jain et al demonstrated that patients who have one-level or two-level posterior lumbar fusions and chronic opioid use before surgery have a 1.2-fold increase in risk for complications including wound complications and all cause 90-day visits to the emergency department.[20] In addition, data from varying studies with longitudinal follow-up demonstrated that up to 87% of patients with regular preoperative opioid use continued with long-term use even after surgery. Patients receiving opioids for 240 or more days within the contiguous year of their surgery were 16 times more likely to continue with postoperative opioid use long term.[21]

In 2023, Reitman et al[2] published a retrospective review to analyze the patterns of opioid use in patients undergoing lumbar surgery for degenerative lumbar spine conditions. The authors of the study found that within their population of focus (e.g., South Carolina Medicaid Patients), 78% of patients undergoing elective lumbar spine surgery were using opioids preoperatively. Moreover, more than three quarters of the patients studied were deemed chronic opioid users and on bivariate analysis, patients with degenerative disk disease in the lumbar spine were more likely to be chronic opioid users and receive higher amounts of opioids during the 30 days after surgery.

Wright et al[22] conducted a single-institution retrospective cohort study to determine whether opioid prescribing practices at discharge were associated with opioid dependence (OD) in patients who underwent

lumbar diskectomy or lumbar laminectomy for degenerative pathology. In total, 819 patients were included in the study of whom 499 (60.9%) of them had an active opioid prescription before surgery. In accordance with data presented by Reitman et al,[2] the most patients with degenerative lumbar spine pathology undergoing lumbar spine procedures preoperatively had chronic opioid use disorder or an active opioid prescription. Furthermore, the study of Wright et al[22] reported that postoperatively, 99.3% of their studied patient population received at least one narcotic prescription within 30 days postoperatively and that 19.8% of them had sustained opioid use 1 year postoperatively. Notably, a new diagnosis of postoperative opioid dependence was observed in 7.5% of previously opioid-naive patients who underwent lumbar diskectomy or laminectomy in this study population.

Reitman et al and Wright et al demonstrated in their respective studies that patients with degenerative lumbar spine conditions have either history of chronic opioid dependence or active prescription opioid use more than 50% of the time.[2,22] Furthermore, both studies highlight the fact that patients undergoing lumbar spine procedures not only typically have preoperative opioid use, but that there is substantial risk for continued opioid use chronically postoperatively. Wright et al highlighted the risk for postoperative opioid dependence in previously opioid-naive patients undergoing lumbar spine procedures. Because of this concern and the demonstrated analgesic effects of cannabis, the use of cannabis as an adjunct to the current multimodal analgesia regimen may help to reduce the risk and duration of opioid use in patients with lumbar spine pathology undergoing intervention.

Cannabis and Lumbar Spine Surgery—Risk of Usage

The goal of the present review is to comment on existing research on the use of cannabis postoperatively for analgesia in lumbar spine surgery given the ongoing challenges with postoperative pain control. One of the more powerful studies to date regarding cannabis use in lumbar spine surgery from D'Antonio et al attempted to demonstrate noninferiority in patients already using cannabis preoperatively who continued the use of it after surgery. Sixty-five cannabis users were propensity matched 3:1 to 194 noncannabis users and then compared. No statistically significant difference was observed in surgical outcomes studies such as fusion rates, preoperative/postoperative patient-reported outcome measures at 6 months to 1 year after surgery, and 90-day readmission rates related to all cause or surgical complications. The important caveat in the study of D'Antonio et al[11] was there was no method to standardize drug administration or ingestion form, and the study instead relied on the patient's self-reported use gathered from retrospective data. Currently, the bar for conclusive, superior therapeutic efficacy does not rest at noninferiority. Paired with data from the study of D'antonio et al and recent literature, cannabis users may experience higher rates of complications and reoperations, which has negatively affected the outlook for marijuana as a pain adjunct in lumbar spine surgery.[23,24]

Moon et al[25] demonstrated in a retrospective review that patients who underwent one-level or two-level posterior lumbar fusion surgery, cannabis use was associated with a lower Charlson Comorbidity Index, a metric to predict 10-year survival in patients with multiple medial comorbidities. Moon et al[26] also reported in a retrospective review using a national inpatient sample database from 2010 to 2014 that patients with identified cannabis use disorder undergoing "spinal fusion" procedures had an increased odds of cerebrovascular accidents and cardiac disease.

Regarding cannabis use in relationship to opioid utilization, Moon et al[25] demonstrated that patients who were cannabis users preoperatively and opioid naïve had increased postoperative prescription opioid usage while in-patient and after discharge. Khalid et al[27] conducted a review of opioid naïve patients undergoing single-level lumbar fusion who either were cannabis users or noncannabis users. Notably, it was demonstrated that opioid naïve patients who were cannabis users used a smaller daily dosage of opioids but had a higher rate of postoperative diagnosis of opioid used dependence when compared with noncannabis users. While not notable, Khalid et al observed that at 6 months postoperatively, opioid utilization was equal among cannabis users and nonusers. More recently, Trenchfield et al performed a retrospective cohort study analyzing the effects of preoperative cannabis usage on postoperative opioid usage after lumbar decompression without fusion. Of significance, Trenchfield et al[28] found that preoperative cannabis usage did not affect opioid consumption.

Barkay et al[29] conducted a retrospective review of patients who underwent single-level lumbar spine fusion between 2010 and 2020 to assess whether patients with concomitant preoperative cannabis usage had more postoperative complications compared with those patients with opioid use disorder or no substance use.

Patients were stratified into one of three study groups: control patients with no opioid use or cannabis use, patients with opioid use disorder, and patients with cannabis usage. Primary outcomes reviewed were complications within 30 days of the index procedure and pseudarthrosis (the lack of bony fusion after spine fusion typically diagnosed 6 months postoperatively) rates at the 18-month postindex procedure. Regarding secondary outcomes, Barkay et al[29] reported an increased risk of experiencing VTE, hypoxia, myocardial infarction, and arrhythmia for both the cannabis and opioid users compared with control subjects. When controlling for tobacco use, the odds of these complications within the cannabis group were no longer notable. Similarly, results suggested a higher rate of pseudarthrosis in the cannabis user group when compared with control subjects; however, when controlled for concomitant tobacco use, the pseudarthrosis rate in the cannabis group was no longer notable when compared with control. This retrospective review highlighted that when analyzing patients using cannabis in the context of lumbar spine surgery, concomitant usage of tobacco must be taken into account when considering possible postoperative complications. To date, no level I evidence study has been conducted or published analyzing the association of tobacco and cannabis with postoperative complication rates.

Expanding on research related to pseudarthrosis after lumbar spinal procedures and cannabis usage, Tao et al[30] evaluated rates of pseudarthrosis in patients who underwent 1-level to 3-level transforaminal lumbar interbody fusion (TLIF) procedures, which are commonly used to achieve nerve root decompression and vertebral fusion. Patients were separated into cannabis users and noncannabis users, and a multitude of demographic factors, medical comorbidities (such as tobacco smoking), and surgical factors were controlled for. Cannabis users were 80% more likely to experience pseudarthrosis within 24 months after 1-level to 3-level TLIF's compared with patients who did not engage in cannabis usage leaving to question if inhalation methods of cannabis consumption lead to risks of pseudarthrosis similar to those known from smoking tobacco products.

Regarding subjective measures, Andre et al compared clinical and patient-reported outcomes (PROs) after transforaminal lumbar interbody fusion (TLIF) in patients who did or did not use cannabis.[31] In this retrospective cohort study, 102 patients who underwent TLIFs were followed for 1 year postoperatively. Patients were categorized based on self-reported cannabis usage and those who did not report cannabis usage. PROs included preoperative Oswestry Disability Index (ODI), 6-month ODI, 12-month ODI, length of stay, complications, return to surgical room, revision surgery, and confirmed fusion. Andre et al found no notable differences in patients with self-reported cannabis usage versus patients without cannabis usage and drew the conclusion that perioperative outcomes were similar in patients who underwent TLIF regardless of self-reported cannabis usage.[31]

Regarding opioid consumption, Kwaczala et al[32] performed a retrospective single-institution study in patients undergoing elective single-level or two-level lumbar fusions and stratified groups based on medical cannabis (MC), recreational cannabis (RC), or nonuser (NU) groups. It was reported that the MC group had markedly higher opioid consumption and surgical site infection rates at 90 days compared with recreational groups and nonusers. Furthermore, Kwaczala et al[32] reported that patients in the MC group not only required higher doses of morphine milligram equivalents (MME) during in-hospital recovery period but also ambulated less and had lower self-reported improvements after surgery than the other two groups. Of note, the RC group was also noted to consume 29% more opioids than nonusers and report a greater level of pain on day of discharge compared with nonusers.

Cannabis and Lumbar Spine Surgery—Benefits of Usage

Although Kwaczala et al reported suboptimal outcomes regarding opioid consumption for MC and RC users, Mirpuri et al[33] in a retrospective cohort study demonstrated contradictory findings in their retrospective cohort study. Cannabis users and noncannabis user cohorts were evaluated, and cannabis users were found to have lower rates of opioid utilization compared with noncannabis users as early as 2 months after one-level to three-level TLIF for degenerative spine disease. Furthermore, cannabis users had lower rates of opioid utilization (>100 MME per day) within the first 14 to 30 days postoperatively.

As mentioned previously, Khalid et al[27] evaluated 454 patients distributed equally into cannabis users and noncannabis users who had undergone single-level lumbar fusions. When assessing daily dosages of opioids, Khalid et al[27] reported that cannabis users had smaller daily dosages of opioids compared with noncannabis user cohorts. This suggests a potential for

decreased opioid utilization from a daily dose standpoint in cannabis user.

Regarding bony healing, Fogel et al, through an animal spine fusion model study, demonstrated no inhibitory effects on bone healing of THC and CBD.[34] When assessing rats who had undergone posterolateral intertransverse lumbar fusion at L4-L5, four study groups providing a placebo (saline), THC and CBD, THC alone, or CBD alone were developed with multiple osteogenic factors measured. Although CBD alone demonstrated upregulated osteogenic factors such as Col1A1 and MMP13, THC alone did not demonstrate any inhibitory effects on bone healing within this spinal fusion animal model.[34]

Discussion

The goal of the present literature review was to understand the pain burden of lumbar spine surgery, and the effects of opioid and cannabis use related to postoperative pain management and overall complication rates after lumbar spine surgery. In addition, we sought to better understand pain pathways related to cannabis usage in patients undergoing spine surgery. It is well documented that lumbar spine surgery is painful postoperatively, and therefore, patients undergoing lumbar spine surgery typically require some form of analgesia such as opioids. As such, we attempt to discuss the potential risks and benefits of cannabis use as a postoperative analgesic adjunct to opioids.

Presently, the authors attempt to provide a balanced review given the available literature. To date, few studies demonstrate clear benefits of using cannabis in patients undergoing lumbar spine surgery who are prescribed opioids for postoperative pain control. Findings reported include decreased daily usage of opioids at 6 months and lower rates of opioid utilization in the immediate postoperative period for cannabis users who undergo lumbar spine surgery.[27,33] An overwhelming amount of research however echoes the conclusions drawn from the retrospective single-institution study of Kwaczala et al, which demonstrated a markedly higher opioid consumption at 90 days in medical cannabis users compared with nonusers.[32] In addition to these findings, higher rates of surgical site infections in postoperative patients undergoing elective single-level or two-level lumbar fusion were also reported for medical cannabis users.[32]

To advocate for cannabis usage as a possible adjunct for pain control in lumbar spine surgery, level I evidence is needed demonstrating the therapeutic efficacy of cannabis without a concomitant rise in postoperative narcotic usage or in postoperative complications related to cannabis. Unfortunately, although the authors presently attempted to provide a balanced review demonstrating the benefits of cannabis use in patients undergoing lumbar spine surgery, there is no clinical study demonstrating purely positive outcomes regarding opioid use, fusion rates, and reduced complications in cannabis users. More so, many current review articles, systematic reviews, and retrospective reviews suggest harmful effects of the patient population undergoing lumbar spine surgery who also engage in cannabis usage.

Concluding Remarks

Presently, the authors of this study provide the most expansive review to date of cannabis use in patients undergoing lumbar spine surgery. Evaluated within this review is the effects of cannabis use on opioid utilization and postoperative complications or benefits. Research at this time supports that patients should be counseled against the use of cannabis as a postoperative analgesic modality because current research demonstrates risks of pseudarthrosis, complications such as surgical site infections, and increased opioid use dependence.[27,30,33] Although there is some research to suggest upregulated osteogenic factors after lumbar surgery in CBD users, these studies are completed in animal models and not human subjects.[34]

For the authors to presently recommend the use of cannabis as an appropriate analgesic adjunct for patients undergoing lumbar spine surgery, more research is required. As future research related to cannabis as an analgesic in spine surgery is completed, competing factors such as concomitant substance use such as tobacco and nicotine, dosing and frequency of cannabinoids, modality of administration of cannabinoids, and the ability to regulate dosing of cannabinoids in patients who engage in recreational usage, will need to be addressed and analyzed. Furthermore, there are ethical considerations and barriers in performing true clinical studies regarding the utilization of cannabis in lumbar spine surgery. The contextual lens through which we can understand what cannabis can provide as a pain control agent is limited to the extent of the populations that we are allowed to study in. Careful consideration that other patient factors such as socioeconomic status, health literacy, and psychosocial stability all have an indirect influence on the results seen in these studies and pose more hurdles that should be recognized. For the time

being however, based on the available studies, cannabis seems to be a "foe" for patients undergoing lumbar spine surgery.

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