

Cannabidiol as Part of Multimodal Pain Management? A Survey of Orthopedic Surgeons' Attitudes and Knowledge

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ABSTRACT

AIM: To assess orthopedic surgeons' knowledge of cannabidiol (CBD) and the extent to which they would be receptive to researching and prescribing CBD.

MATERIALS AND METHODS: An anonymous questionnaire was distributed electronically or in paper form to all 126 orthopedic surgeons at an orthopedic specialty hospital between June 5, 2019 and September 24, 2019. Surgeons were asked to provide demographic information, indicate familiarity with CBD, and express views regarding perioperative CBD use in the context of clinical practice and research.

RESULTS: Out of 126 questionnaires, 94 were returned and evaluated. Most surgeons (86%) had some familiarity with CBD, though 68% did not know whether CBD would be a useful adjunct in the perioperative recovery process. The vast majority expressed interest in learning more about CBD (83%), studying CBD (88%), and recommending CBD to patients if shown to be opioid-sparing or NSAID-sparing (85%). Contingent upon further studies, no surgeons were categorically opposed to recommending CBD as part of a multimodal pain regimen.

CONCLUSION: The overall positive view of CBD by surgeons opens the door to future research which would elucidate the safety and efficacy of CBD in the orthopedic perioperative setting. If CBD is shown to be opioid-sparing, prescribing CBD may represent a solution to the ongoing opioid epidemic and change the pain management paradigm across various medical specialties.

Key words: Cannabidiol; Orthopedics; Surgeons; Surveys and questionnaires; Postoperative pain

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INTRODUCTION

Treating pain after surgery has traditionally relied on the administration of opioids, with orthopedics accounting for over 12 million opioid prescriptions in the United States from July 1, 2016 to June 30, 2017^[1]. However, accelerated by the opioid epidemic and a

desire to overcome this public health problem, increasing focus has been placed on the employment of multimodal approaches to reduce or even eliminate opioid consumption. To date, evidence suggests that patients suffer fewer complications when non-opioid analgesics are employed though drugs beyond non-steroidal anti-inflammatory medications and cyclooxygenase inhibitors have limited value in a multimodal pathway^[2]. Supported by sound preclinical evidence^[3-5], cannabidiol (CBD), a non-intoxicating cannabinoid, has been increasingly used by the general public to treat various conditions including pain as well as sleep and mood disorders^[6-8]. Although its anti-inflammatory and analgesic properties have been well documented in animal models, clinical studies investigating the efficacy of CBD in reducing orthopedic post-surgical pain and inflammation are missing to date. Despite limited FDA approval to treat childhood seizures, approximately 14% of Americans 18 years and older are estimated to be using CBD, citing relief from pain as the primary reason for use^[9]. In this consumer driven environment, it remains unknown to what degree clinicians, and especially orthopedic surgeons are familiar and/or comfortable with its use in the perioperative period. To elucidate this topic, we designed a questionnaire and distributed it to 126 orthopedic surgeons in a single institution. We hypothesized that surgeons would have limited knowledge of but would generally have positive attitudes towards perioperative CBD use.

METHODS

An anonymous, 11-item questionnaire was designed to collect basic demographics and information on familiarity with, attitudes towards and concerns regarding the use of CBD in postoperative patients. The study received Institutional Review Board exemption and participation was voluntary. Questionnaires were distributed electronically via REDCap (supported by NIH Award Number UL1TR002384) or in paper form to all 126 orthopedic surgeons at an orthopedic specialty hospital between June 5th, 2019 and September 24th, 2019. An introductory text was sent with the survey describing CBD and its non-intoxicating nature, and the premise of the study.

The individual survey items can be found in Table 1. Provider type was assessed by asking respondents to select their primary service at the hospital: Joints, Sports, Hand/Foot, Spine, Pediatrics, Trauma, or other with the option to enter a response. Professional tenure was assessed by the number of years in practice ranging from less than five, 6-10, 11-15, 16-20, 21-25 or greater than 25. The survey consisted primarily of short questions, for which participants were able to select Likert-type or yes/no/I don't know options to represent their familiarity and attitudes towards CBD. A free-text box was provided for participants to enter their concerns regarding CBD.

RESULTS

Out of 126 questionnaires, 94 were returned and evaluated^[10]. Of the respondents, the majority of surgeons were joint arthroplasty orthopedists or specialized in sports medicine. Surgeons' years in practice spanned from less than 5 to more than 25 years. Respondent characteristics are summarized in Table 2. Most surgeons (86%) had some familiarity with CBD with only 4% claiming to be very familiar with this agent. None of the participants thought that CBD might harm the recovery process, while 27% thought it to be a useful adjunct and 68% said they did not know. Of those reporting CBD to be a useful adjunct, the majority thought it was either moderately to very useful (68%). 77% of surgeons agreed or strongly agreed with the use of CBD if a patient or another healthcare provider suggested

its inclusion in the care process. The vast majority of surgeons expressed interest in learning more (83%), studying (88%) CBD further or using it if it were to be shown that it was opioid and/or NSAID sparing (85%). No surgeons were categorically opposed to using CBD as part of multimodal pain management if shown to be beneficial with minimal side effects; 24% of surgeons listed concerns with the use of CBD that they would like to be addressed. These included issues regarding safety, abuse liability, positive drug tests for athletes, lack of clinical data and lack of education (Supplemental Table 1).

Table 1 Questionnaire Distributed to Orthopedic Surgeons.

| |
|---|
| What is your primary service? |
| How many years are you in practice? |
| How familiar are you with CBD? |
| Do you believe CBD is a useful adjunct during a patient's recovery from surgery? |
| If yes, how useful do you believe CBD is as an adjunct during a patient's recovery from surgery? |
| Do you believe CBD is harmful to a patient and his/her recovery process? |
| If yes, how harmful do you believe CBD is to a patient and his/her recovery process? |
| If a patient or another provider requests inclusion of CBD in a postoperative multimodal regimen and if side effects are minimal, would you agree to its use? |
| Would you be interested in learning more about CBD? |
| Would you be interested in seeing CBD studied in the perioperative and recuperative setting? |
| If CBD would be shown to be opioid or NSAID sparing, would you be in favor of recommending it to patients? |
| Assuming potential benefit and minimal side effects, would you direct a patient to take CBD postoperatively as part of a multimodal pain regimen? |
| Do you have any concerns regarding CBD? |
| If yes, what is your biggest concern? |

Supplemental Table 1 Surgeons' Concerns Regarding CBD.

| |
|--|
| Safety |
| Known and unknown short-term and long-term side effects or interactions (n=8) |
| Potential for psychological dependence, abuse, addiction, and apathy (n=4) |
| Potential for increased fall risk after THR/TKR |
| Potential effects on bone healing |
| Gateway to other drug use behavior (e.g., THC) (n=2) |
| Given it is being portrayed as innocuous, what would the argument be against chronic use (more than 6 weeks after surgery) |
| Variability and poor quality assurance of the different formulations of CBD |
| Lack of Clinical Evidence |
| Unknown dosing, consistency, and mechanism of action |
| Lack of regimented formula and clinical evidence of its efficacy for perioperative needs |
| Lack of data on the efficacy of CBD compared to that of currently available non-narcotics |
| "No good science behind it-a myriad of indications a mile wide makes me suspicious" |
| "It is more hype than hope and that in the process generates profit" |
| "As a pediatric orthopedic surgeon, I'm not sure I see this as useful for my practice" |
| Legal/Regulatory |
| Perception, stigma, and legality of CBD (n=2) |
| Approval from WADA, NCAA, USOC, IOC |
| Drug testing for athletes |

Table 2 Respondent Characteristics

| Primary Service, n (%) | |
|--------------------------|-----------|
| Joints | 35 (38) |
| Sports | 21 (22.8) |
| Hand/Foot | 12 (13) |
| Spine | 11 (12) |
| Pediatric | 5 (5.4) |
| Trauma | 5 (5.4) |
| Other | 3 (3.3) |
| Years in practice, n (%) | |
| Less than 5 | 9 (9.8) |
| 6-10 | 10 (10.9) |
| 11-15 | 15 (16.3) |
| 16-20 | 13 (14.1) |
| 21-25 | 21 (22.8) |
| Greater than 25 | 24 (26.1) |

DISCUSSION

Surveyed orthopedic surgeons expressed generally positive attitudes towards the perioperative use of CBD in their patients but expressed a desire for further study to address efficacy and safety. Though they were not asked to specify their rationale, surgeons who perceived CBD as a potentially useful adjunct may have been aware of the anecdotal evidence suggesting that CBD may be used to reduce chronic and arthritis/joint pain, relieve anxiety and depression, and improve sleep with minimal side effects^[6]. These patient-reported outcomes are key factors that affect the quality of the orthopedic surgery recovery and pain management process and overall patient satisfaction^[11-13]. Even though anecdotal evidence is difficult to validate, may inadequately control for confounders, and is prone to self-selection bias, the mounting personal accounts of CBD's purported benefits and growing consumer demand, particularly for pain relief, cannot be ignored. The United States has been facing a worsening opioid crisis, which has claimed nearly 500,000 lives from 1999 to 2019 according to the Centers for Disease Control and Prevention (CDC), that can be attributed in part to opioid prescribing practices and opioid misuse by patients across various medical specialties^[14]. With the opioid crisis in the context of orthopedic surgery at the forefront of their minds, surgeons may be more receptive to clinical research that would investigate CBD's potential as an alternative to opioids or as an adjunct in an opioid-sparing perioperative pain management regimen with the long-term goal of reducing or eliminating opioid use. The willingness to conduct such research is representative of a culture of innovation and leadership in creating new solutions to the opioid crisis, improving patient outcomes, and pioneering the future of pain management practices, which are collective interests of the medical community.

Given the lack of clinical data regarding the safety and efficacy of CBD when used in the orthopedic perioperative setting, it was expected that a large proportion of surgeons, who rely primarily on scientific, peer-reviewed studies, especially randomized controlled trials, to inform their perspective on any medication use, would respond to the survey questions with uncertainty. In fact, prior to administering the survey, clinical studies of the opioid-sparing effects of adjunctive CBD use were unreported and studies involving the use of CBD to treat pain demonstrated context-dependent (e.g., cohort size, disease state, dosage, route of administration) variability in efficacy^[15-17]. Newer studies suggest that CBD may help reduce

and eliminate opioid use, relieve chronic pain, treat anxiety and depression, and improve sleep quality, which would improve the quality of life of orthopedic surgical patients^[18,19].

Studies published both before and after the survey was administered have demonstrated in murine and canine models that CBD relieves neuropathic pain, inflammation, and swelling associated with osteoarthritis^[5,20]. While the effects of CBD on inflammation have yet to be studied in randomized controlled trials involving human subjects, the anti-inflammatory effects of CBD^[21] may aid in reducing joint stiffness and pain resulting from orthopedic surgery, thereby improving orthopedic post-surgical outcomes such as rehabilitation, joint mobility, ambulation, skeletal muscle strength, and range of motion^[22]. Early post-operative physical therapy and rehabilitation – unburdened by prolonged post-surgical inflammation with associated pain – is key to minimizing recovery time and restoring function^[23,24]. A phase I, randomized controlled trial assessing the safety profile of CBD has indicated that CBD is generally well-tolerated at dosages up to 1500mg/day with no severe adverse events reported^[25]. This contrasts with NSAIDs, which have been associated with gastrointestinal, cardiovascular, and renal complications and a potential negative effect on bone healing^[26-29]. Furthermore, compared to other cannabinoids, such as THC, CBD does not produce any euphoria, intoxication, or physical dependence – qualities that may make it more acceptable to patients, physicians, and regulatory agencies^[25].

During the study time frame, when responding to the survey, surgeons may have also taken into consideration recent historical events which effectively lifted legal and regulatory barriers to clinical trials investigating CBD^[30]. In 2018, Epidiolex®, an oral solution of purified CBD, became the first cannabis-derived medication to be approved by the FDA and was reclassified by the DEA to Schedule V. In addition, hemp, a type of cannabis with a THC content less than 0.3%, was removed from the Controlled Substances Act. These regulatory and legal changes reflect the progressive contemporary attitudes towards cannabis which have gradually shifted towards tolerance and acceptance^[31]. Considering the legalization, FDA-approval, and DEA re-scheduling of Epidiolex®, surgeons and medical professionals, in general, may now be more receptive to conducting CBD research in the perioperative setting. As of 2020, Epidiolex® is no longer a controlled substance.

Limitations of the survey include lack of validation, and sampling from a single, high-volume urban institution. As a result, the responses are open to some degree of interpretation, and the overall conclusions may not be reflective of attitudes of orthopedic surgeons more generally. Future qualitative studies may investigate the sources of information which healthcare and medical professionals have used and plan to use to educate themselves about CBD and how knowledge gained from these sources and emerging literature impact perspectives on CBD. Extension of surveys to other orthopedic surgeons throughout the country and world, potentially through professional organizations, may offer a more comprehensive overview of perspectives on CBD.

CONCLUSION

In summary, this environment suggests that additional studies on CBD in the clinical setting are warranted. If successful, CBD represents a potential alternative to traditional pain modulating agents. Due to its well-tolerated, non-opioid and non-intoxicating nature, it holds promise especially for use in patients who may be at particularly high risk when exposed to opioids or NSAIDs. As more

peer-reviewed clinical trials involving CBD are published, finding the right timing and variety of means for presenting the research findings and educating surgeons about CBD will be critical for the future of CBD use in the perioperative setting – whether for further research or for treating patients in clinical practice.

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