



Implications of Cannabis Use for Patients Undergoing Office-based Anesthesia and Oral and Maxillofacial Surgery

Introduction

Cannabis, widely known as marijuana, comes from the Cannabis sativa plant. It is the most used “drug” worldwide, with more than 180 million reported users across the globe in 2018.¹ In the U.S., cannabis remains a federally classified Schedule I substance. However, multiple states have legalized its use for medicinal and recreational purposes, leading to an increase in its popularity – particularly among the younger population with 36 percent of 12th graders and 43 percent of college students reported having used it in the past year.²

The origin of the cannabis plant can be traced back to Central Asia, where its properties were used for recreational, medicinal and religious purposes. Compounds that exert these properties are referred to as “cannabinoids.” These compounds can be classified as phytocannabinoids (produced by plants), endocannabinoids (produced by animals and humans) and synthetic cannabinoids (manufactured).³

Cannabis contains hundreds of compounds, and two of its major active ingredients are tetrahydrocannabinol (THC) and cannabidiol (CBD). THC induces the euphoric and psychoactive effects of marijuana. CBD is the non-psychoactive ingredient that can be used to treat some forms of epilepsy, chronic pain and inflammation.⁴

Although cannabis has been touted for its beneficial effects such as pain and anxiety control, it also has the potential for adverse physiologic effects, primarily on the respiratory and cardiovascular systems.⁵ With the changing legal landscape regarding cannabis, its prevalence is expected to continue to increase; therefore, providers who are involved in the care of patients who use cannabis need to be well-informed.

Oral and maxillofacial surgeons perform multiple daily procedures using local anesthesia sedation, general

anesthesia or a combination of both. Invariably, encounters with cannabis users will occur. Therefore, OMSs need to be prepared and understand how to best manage these patients. This paper will discuss the pertinent physiologic and pharmacologic effects of cannabis, its potential interactions with common medications used in the office setting and potential challenges that OMSs may face in managing patients who use cannabis.

Different Forms of Cannabis for Intake

Marijuana is commonly used and abused. Patients may be taking medically prescribed cannabis products or self-administered forms of cannabis. Some patients are chronic users, and others are more occasional. For susceptible individuals, it can be very addictive. While some states in the U.S. have legalized cannabis, many have no real requirements for purity testing or quality. It is essential that OMSs have a good understanding of the various forms and strengths of cannabis and how that can impact complications under sedation and general anesthesia.

In general, there are three traditional forms of cannabis: herbal, hashish and hash oil. Herbal cannabis is made from the flowers and other parts of the Cannabis sativa plant. Hashish is made from cannabis resin and is a much stronger and more concentrated substance that can contain three to five times higher levels of THC, the most active component. Hash oil is even more concentrated. All these substances often contain significant amounts of impurities and can be intentionally laced with other illicit substances, which may be unknown to the user.

Cannabis can be smoked alone or in combination with tobacco in various ways, including as a handmade cigarette or joint, or using bong, pipes, vaping and other electronic devices. Hash oil can be mixed with alcohol. Any of the forms of cannabis can be mixed into edible products such as candy, cookies, gummies, honey, jelly, ice pops and syrups. Topical forms of cannabis are widespread and used

as lotions, balms and creams to treat arthritis, injuries to joints, and muscle spasms and aches. In those uses, THC does not generally reach the bloodstream.

However, when used in a long-wearing patch, THC can be absorbed systemically, and the user can have physiologic effects.⁶ THC produces many physiologic changes in neurologic, cardiac and pulmonary functions. There is wide variability in THC levels in various cannabis products. Over recent decades, the THC content has increased dramatically in available cannabis products. In the 1980s, THC potency was around 2 percent; in the 1990s, it was around 4 percent; in recent years, it is around 10 percent. Low levels of THC produce euphoria, but higher doses can cause hallucinations and extreme paranoia.

Pharmacologic Effects of Cannabis

The pharmacologic effects of cannabis result primarily from THC, but there are at least 100 other pharmacologically active cannabinoids in cannabis. Cannabinoid receptors are found in the central nervous system, leucocytes, gastrointestinal tract, spleen, endocrine glands, arteries and heart.¹ There are two known cannabinoid receptors, labeled CB1 and CB2.

The pharmacology of cannabinoids is very complex, and there is much that is not fully understood. Numerous topics of research are ongoing on the pharmacologic effects on humans, both adolescents and adults, but it will be years before there is a good understanding. Future research may provide improved insights into how THC interacts with other medications, including anesthetics used in office-based sedation and general anesthesia.

Physiologic Effects of Cannabis

Endocannabinoid System

Cannabis interacts with the endocannabinoid system (ECS), which consists of endogenous lipid mediators (endocannabinoids) and G-protein-coupled cannabinoid receptor 1 (CB1R) and cannabinoid receptor 2 (CB2R). CB1R is found throughout the nervous system as well as the heart and vascular smooth muscle. It is the primary receptor responsible for the psychoactive effects of cannabis. CB2R is found in the immune and hematopoietic cells and is responsible for the anti-inflammatory effects.^{4,6} Humans produce endocannabinoids such as anandamide and 2-arachidonoylglycerol which are agonists for CB1R and CB2R. Phytocannabinoids (e.g., THC, cannabidiol)

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and synthetic cannabinoids also interact with CB1R and CB2R.⁶

Cardiovascular Effects

Cannabis can exert its effects on the cardiovascular system via activation of the sympathetic system and suppression of the parasympathetic system. This manifests in tachycardia and a slight elevation in supine blood pressure.⁴ The tachycardia can occur within 10 minutes of smoking cannabis and last between two and three hours. There can be a 20 to 100 percent increase in heart rate.⁷ It is postulated this is due to the activation of the sympathetic system with an increase in levels of sympathetic neurotransmitters by cannabis.⁴

Additionally, cannabis reduces vagal slowing during the Valsalva maneuver, suggesting suppression of the parasympathetic system. However, in some animal studies, cannabinoid agonists resulted in bradycardia and hypotension suggestive of parasympathetic stimulation.⁷ One study did not show any change in hemodynamics when high-dose THC was given orally over the course of six to 13 days.⁴ These contradicting results suggest the true hemodynamic effects of cannabis remain uncertain; however, it has been postulated that lower doses can cause sympathetic stimulation while higher doses results in parasympathetic stimulation.⁷

Higher doses of marijuana also have been shown to cause postural hypotension and dizziness in healthy volunteers through a decrease in cerebral blood velocity via transcranial Doppler, potentially leading to an increased risk of ischemic strokes.⁷ However, a population-based study of almost 50,000 Swedish men found no association between cannabis use and stroke when confounding variables were considered.⁴

Cannabis use can lead to an increase in myocardial oxygen demand and a decrease in the supply of oxygen to the heart. The tachycardia causes an increase in work for the heart, while the inhalation of marijuana causes an increase in the levels of carboxyhemoglobin and a reduction in oxygen supply.^{4,7} This can lead to a transient myocardial



ischemia as shown in a study of patients with known chronic stable angina who had never previously smoked marijuana where after smoking one cannabis cigarette had a decrease in the time from exercise-induced angina by nearly 50 percent.⁴ There are multiple case reports and retrospective studies that suggest a correlation between cannabis use and myocardial adverse events; however, there have been no prospective studies that have shown a strong association between cannabis use and long-term cardiovascular outcomes.⁴

Some studies have suggested that cannabis use may cause arrhythmias, primarily atrial fibrillation; however, this remains inconclusive, and there is still uncertainty regarding the association of cannabis and arrhythmias.⁴

There are limited data on the cardiovascular effects of cannabis use in the perioperative period, although the few available studies suggest an increased risk of tachycardia, arrhythmias and myocardial infarction.⁵

Respiratory Effects

Smoking cannabis can cause bronchodilation in the acute period, although the mechanism is not well understood. The bronchodilation peaks at 15 minutes and lasts for one hour. With chronic use, cannabis can cause inflammation of the airways, leading to an increase in sputum production, wheezing, coughing and lung infections. Regarding chronic obstructive pulmonary disease (COPD), there is a lack of evidence to find a causal role for regular cannabis use and the development of COPD, with studies showing both an increase and decrease in airway obstruction from cannabis use. Lastly, available evidence has not shown that chronic cannabis use can cause lung cancer.⁸

Gastrointestinal, Endocrine, and Immune Effects

Cannabinoids can be effective treatments for chemotherapy-induced nausea and vomiting; however, THC has not been shown to prevent postoperative nausea and vomiting. There is an increasingly recognized complication of chronic cannabis use termed “cannabinoid hyperemesis syndrome,” which is characterized by recurrent nausea, vomiting and abdominal discomfort.¹ Acute THC use can result in insulin resistance,¹ and chronic cannabis use can lead to increased risk of prediabetes.³⁰ Other endocrine effects of chronic cannabis use include reduced sperm function, reduced fertility and a decrease in thyroid hormones.³

CB2R can be found on immune cells and exert anti-inflammatory effects; however, there is no indication the use of cannabis can lead to systemic immunosuppression.¹

Neurologic Effects

Cannabis has been shown to be effective at treating some seizure disorders. However, it also can have a detrimental effect on the central nervous system, primarily the potential to cause a decrease in cognitive function with long-term use. Abstinence may revert the cognitive impairment.^{1,2} Cannabis use can increase the risk of psychosis and suicidal ideation and suicide attempts.¹

Cannabis is commonly used to reduce chronic noncancer pain; however, a meta-analysis did not show a significant reduction in pain on a visual analogue scale when cannabinoids were compared to placebo.¹ Another meta-analysis found no role for cannabinoids in the management of acute pain. Furthermore, there is emerging evidence that chronic cannabis use is associated with increased postoperative pain and opioid use.¹

Anesthetic Drug Interactions

To date, several perioperative recommendations are based on case reports and anecdotal information. Current publications also tend to be offering recommendations on THC products that are less potent than the marijuana some patients are using. Until OMSs undertake studies using THC concentrations their patients are using, only extrapolations from poor data and common sense are left.

Can marijuana be used to premedicate anxious patients? Gregg et al. published two papers using THC to test this hypothesis. Intravenous THC resulted in increased anxiety, dysphoria and paranoia for third molar patients. Intraoperatively, tachycardia was reported. The duration depended upon the IV dose of THC and lasted 75 minutes for a THC dose of 0.022 mg/kg and 100 minutes for a dose of 0.044 mg/kg THC IV. THC would not be beneficial as a premedication when compared to a benzodiazepine.

A second study looked at five patients who smoked marijuana within 72 hours of surgery. There was a

64.8 percent increase in heart rate that took 38 minutes or longer to return to baseline. The control group heart rate was 39 percent above baseline and took 19 minutes to return to normal. Cardiovascular side effects limit the usefulness of THC for premedication.^{1, 9, 10}

Marijuana Case Reports and Interactions with Anesthetic Agents

The variations in THC concentrations in the available marijuana products can be anywhere from under 10 percent to up to 90 percent. Additionally, the variability of frequency of usage and routes of ingestion also add to ambiguity in interactions with anesthetic agents. Further, time lapsed from the last use of a marijuana product pre-operatively may also be a factor that influences drug interactions.

Propofol Interactions with Marijuana

There are conflicting reports about the interactions between propofol and marijuana. THC and propofol are metabolized by CP450 enzymes. These enzymes can be upregulated by the chronic use of marijuana and increase the metabolism of anesthetic agents. Flisberg et al. studied men between the ages of 18 to 50 who used marijuana more than once a week and its effect on propofol induction dosing. The induction dose needed to place an LMA was greater in the marijuana group. However, the dose needed to obtain a BIS < 60 was comparable in both groups.⁴

In a study by Imasogle et al. (2021) with 318 patients – with 167 using marijuana daily (four of seven days per week), weekly (one to two days per week) and occasionally (less than once per two months) – undergoing endoscopy under moderate sedation, it was found that marijuana users required more propofol than nonusers. The daily users required more than the weekly or occasional users.⁵ (See Table 1.)

In a contradictory study, King et al. examined moderate sedation medications for esophagogastroduodenoscopy. The study involved 23 marijuana patients – nine daily use; seven weekly/monthly and seven no frequency reported – who were compared to controls. There was no difference in propofol, fentanyl or ketamine between the groups.⁷

Other contradictory case reports also have shown no increase in the dose of propofol with marijuana users.³ Most of the case reports and anecdotal reports conclude that marijuana users require higher induction doses of propofol. However, maintenance dosing is still up

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for debate. Reliable data using THC dosing found in commercial flower, shatter, wax and other concentrates have not been studied to make real clinical judgments.

Opioid Interactions with Marijuana

The analgesic effect of marijuana is partially mediated by opioid delta and kappa receptors. There is a resultant synergistic effect between marijuana and opioids that may have clinical implications. Marijuana inhibits CYP34A enzymes, which can result in central nervous system and cardiovascular depression from the combination of the anesthetic agents and marijuana. Decreased metabolism of oxycodone, hydrocodone and fentanyl has been reported as well.^{2, 6, 11, 12, 13}

Endoscopic sedation studies have concluded that marijuana users required 14 percent more fentanyl and 19.5 percent more midazolam than non-users. However, if the total dose of each drug is considered, the difference between users and non-users is similar to normal patient to patient variations in anesthetic drug dosing.¹⁴

Other case reports find no increased dosing of fentanyl for anesthetic procedures. Clinically, it seems prudent to reduce the dose intraoperative fentanyl or use infusions of remifentanyl.³

Postoperative Pain Management with Opioids

Marijuana seems to be beneficial as an adjunct for chronic pain management. However, reports to date find marijuana patients needing increased opioid dosing to manage acute postoperative pain.^{2, 10, 13}

Other Anesthetic Agents

The literature is sparse regarding marijuana interactions with other anesthetic agents. The reports suggest no dose adjustments for dexmedetomidine, ketamine or desflurane. Like opioids, marijuana daily use may have a hyperalgesia component, so ketamine's effect on NMDA receptors may become useful during anesthesia. There may be more emergence phenomena with ketamine-marijuana, thus the need to intervene with dexmedetomidine. The data on midazolam is conflicting to date. There may be a need

to reduce the dose because of CNS depression. Another report shows no difference for marijuana vs. non marijuana users.

There is emerging evidence that marijuana users may develop tolerance to sevoflurane, so an increased MAC is indicated.¹⁵

One literature review suggests the avoidance of ketamine and sympathomimetic agents if the marijuana patient presents with tachycardia, hypertension or dysrhythmias. While the recommendation seems practical, clinicians need to ask why they would be anesthetizing that patient regardless of marijuana use.¹¹

Clinical Challenges with Office-based Anesthesia

Patients using marijuana are coming into OMS offices for surgery and anesthesia every day. Anecdotal reporting on difficult anesthetics is abundant. OMSs are faced with multiple challenges with these patients yet have few concrete answers. This section will address these concerns and hopefully increase the ability for OMSs to provide safe anesthetic care.

Preoperative Evaluation

The preoperative history must include questions about cannabis use. The clinician will evaluate the frequency of use, the products used by the patient and the method of delivery. Is the patient using marijuana monthly, weekly or daily, and is that daily use multiple times per day? Patients using marijuana infrequently (monthly) are less apt to have anesthetic interactions than the daily user. The patient can be categorized as a naïve user, chronic user, or a marijuana heavy user or marijuana use disorder patient.

What type of product is the patient using? Flower products are typically smoked by a cigarette (joint), pipe or water pipe. The THC content in these products is variable, especially with “street” grade marijuana. Commercial grade flower and the marijuana concentrates have a higher concentration of THC and will have greater interactions with anesthetic agents. If a patient is using commercial marijuana for medicinal purposes, the clinician should document the THC content. The most dangerous cannabis product regardless of surgery and anesthesia is the new psychoactive compound, K2/Spice. (See Table 2.)

Each patient’s comorbidities must be identified because of potential interactions with cannabis. Patients with

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chronic bronchitis, asthma or COPD can have symptoms exacerbated by cannabis. The smoke – along with high combustion temperature – can precipitate laryngospasm and bronchospasm. That risk can last up to four hours after smoking. Marijuana carboxyhemoglobin levels are five times that of tobacco smoking, so less oxygen binds to hemoglobin resulting in shorter times to desaturation.

Middle-aged patients with coronary artery disease can have chest pain secondary to the increased tachycardia and myocardial oxygen consumption induced by cannabis. Anginal patients should be asked about anginal free functional capacity before and after marijuana use. High-dose concentrates in these patients can increase the risk of an acute myocardial infarction as well, especially within the first hour of marijuana consumption. A study of 1,913 adult patients with a history of a prior myocardial infarction had a 2.5 times greater risk of death if they used marijuana one time per week and a four times greater risk of death if they used marijuana more often. Practitioners should have a low threshold for preoperative medical consultations. (See Table 3.)

New users will present with tachycardia that may range from a 20 to 100 percent increase in heart rate. This is mediated by increased sympathetic activity and down regulation of parasympathetic activity. Chronic users may be tachycardic and hypertensive, or they can have bradycardia and postural hypotension. Physical examination should include BP and pulse and for chronic users, an ECG rhythm strip to identify symptomatic palpitations.^{2, 6, 7, 11, 12} (See Table 4.)

Patients often use other recreational drugs in addition to marijuana. The practitioner must inquire about other agents as well. At the consultation visit and preoperatively, the doctor needs to be alert to signs of acute intoxication. While low-dose THC typically causes euphoria, relaxation and relief of anxiety, intoxicated patients and some naïve users can present with anxiety, dysphoria, psychosis, and impaired cognition and coordination. Physical signs will include tachycardia, increased blood pressure, tachypnea, airway reactivity and ataxia. These patients may have

delayed awakening, postoperative agitation and delirium. Elective surgery is contraindicated until those symptoms subside.¹⁶

Marijuana Prior to Surgery

Elective surgery should be canceled for patients who are acutely intoxicated from marijuana. There are currently no studies that stratify risk for patients who may have used marijuana closer to the time of surgery or recommendations on when patients should abstain from the use of marijuana before an anesthetic. A typical marijuana cigarette in the United States weighs 300 to 325 mg of plant cannabis. Its THC content can range between 15 to 30 percent. A patient using marijuana in this dose once a month or week should not experience withdrawal from stopping before surgery. A 72-hour period will allow for a decrease in carboxyhemoglobin levels, airway reactivity and cardiovascular irritability. Even refraining from using the marijuana for 48 hours should have some benefit with little risk to the patient.

The cardiovascular and respiratory effects of preoperative marijuana have been discussed. Three references state that marijuana should be stopped for 72 hours preoperatively to allow cardiovascular and airway irritability to subside. However, there are no studies to compare stopping for 72 hours vs. not stopping preoperatively. The *British Journal of Anaesthesia* in 2021 did make preoperative recommendations for marijuana users and surgery. Patients consuming more than 1.5 grams of smoked cannabis a day, greater than 20 mg of THC oil, or any unknown cannabis product more than two or three times a day should be considered for weaning the dose preoperatively. Weaning should be considered if there are more than seven days before surgery. There was no consensus for one to six days before surgery, and weaning should not be considered if there is only one day before surgery. No specific weaning protocol as it relates to dose was described.¹⁷

Intraoperatively, the authors recommended additional PONV prophylaxis along with a greater depth of anesthesia for induction and maintenance. For the heavy marijuana user, the British study opened the door for preoperative modifications. The heavy marijuana user: daily use of flower, multiple daily use of flower, or the use of concentrates throughout the week should require some weaning. A week before surgery if the dose can be reduced

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by 25 percent the first two days, then by 50 percent the remaining days preop, this should reduce the respiratory and cardiovascular effects of the drug. At least three days before surgery, the product should not be smoked, it should be oral or at least vaped to reduce lung irritation. They recommend that postoperatively, the patient can return to their normal dose but by mouth or at least vaping to reduce heat to wound.

Medicinal marijuana should be continued for patients. No adjustments should be made without consulting the physician. Hospitalized patients will require a pain management consultation to see if a synthetic cannabinoid can be added for these patients.

Marijuana Withdrawal

Abruptly stopping marijuana can result in withdrawal symptoms. While men are more frequent users of marijuana, women are more likely to suffer severe withdrawal symptoms. Withdrawal usually has an onset of 24 to 72 hours with a peak after one week and resolution in about two weeks. Withdrawal in daily users of marijuana is far more frequent than non-daily users. Heavy marijuana users – especially daily users, multiple times a day with high-potency marijuana – can develop withdrawal in 24 hours. (See Tables 5 and 6.)

This information clearly shows that stopping marijuana for 72 hours in heavy, daily users is contraindicated. The practitioner needs to perform a comprehensive preoperative examination for the marijuana patient to assess risks and benefits.^{17, 18, 19}

While many OMS practices perform open airway anesthesia with mini boluses of medications, the marijuana patient is prone to “rocky” or “combative” anesthetics in the office. This group of patients will benefit from establishing a deep level of sedation and maintaining them in that state. This is best accomplished using an infusion pump where OMSs establish and maintain a consistent plane of anesthesia.

Conclusion

The use and abuse of cannabinoid products are increasing in the United States. The current THC levels in legal and illegal marijuana is much higher than historically seen. Additionally, marijuana users may be using other legal and illegal intoxicants simultaneously. The marijuana user poses a unique challenge in open-airway sedations and general anesthetics practiced most by OMSs. These patients will need higher doses of benzodiazepines, opioids and hypnotic sedatives to reach a deeper plane of anesthesia. Further, chronic use of marijuana leads to physiologic functional imbalances that may make these patients unsafe candidates for office-based sedation. Careful patient selection and a thorough understanding of the effect of marijuana on normal physiologic function – as well as the knowledge of interactions between commonly used drugs and marijuana – will help clinicians manage this subset of patients safely in their offices.

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Table 1

Sedation Medications Needed for Cannabis Users Versus Non-users

Sedation	Non-Cannabis Users 255 patients	Cannabis Users 25 patients	Difference in Dose	% Increase in Dose Needed
Fentanyl (mcg)	109.91	125.93	25 mcg	14%
Midazolam (mg)	7.61	9.15	3 mg	19.5%
Propofol (mg)	13.83	44.81	30 mg	220.5%

Adapted from Reference 20

Table 2

Cannabis Products: Frequency and Techniques of Use

Frequency	Technique	Marijuana Product
Monthly (infrequent use)	Smoking	Flower
Weekly	Vaporize or Dab	Concentrate
Daily	Vape Pen	K2/Spice
Multiple times a day	Edibles	Medical Marijuana and THC Dose

Reference 4



Table 3

Signs and Symptoms of Concern on History and Physical

Medical History	Cannabis User	Comorbidity
Questions & Answers	Cough, Sputum, Wheeze	Asthma, Bronchitis, COPD
	Chest Pain & Palpitations	CAD
	Dysrhythmias → A-fib, PSVT, Atrial Flutter, PVCs, 2nd degree AV block, and VT	CAD
Use of Other Recreational Drugs		
Hyperemesis with Chronic Marijuana Use		

Reference 4

Table 4

Signs and Symptoms Seen in New, Naïve and Chronic Users

New User	Tachycardia within 2 hours MH use
Naïve User	↑ SBP within 2 hours MH use
	Dysrhythmias: AFib, Aflutter, PVCs, PSVT, AV Block, VT
	Dyspnea, Sputum and Wheeze
Chronic User	Bradycardia or Tachycardia
	Orthostatic Hypotension
	Dysrhythmias
	Hyperactive Airway
	Dyspnea, Sputum and Wheeze

References 4, 13, 15



Table 5

Withdrawal in Heavy Users of Marijuana

Typical Products of Heavy Users	High potency flower, marijuana concentrates, synthetic K2/Spice, multiple times per day
Onset	Day 1
Peak Symptoms	Day 4 (range of 1 to 8 days)
Resolution of Symptoms	Greater than 16 days

References 1, 8, 21, 22

Table 6

Marijuana Withdrawal in General

Signs and Symptoms	Frequency
Sleep Difficulty	14% Most reported symptom
Irritability	14%
Anxiety	13%
Headache	12%
Depressed Mood	11%
Physical Descriptions	
Irritability, Anger, Aggression	
Anxiety, Nervousness	
Insomnia, Restless, Depressed Mood	
Abdominal Cramps	
Tremors	
Sweating, Fever, Chills	
Headaches	

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