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Perioperative Considerations of Cannabis Use on Anesthesia Administration

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INTRODUCTION

As of 2018, an estimated 9.5% of the United States adult population were cannabis users.[1] This percentage has likely continued to increase with the use of both recreational and medicinal cannabis in the United States. The use of medical cannabis is currently legal in 37 states, and recreational cannabis use is legal in 18 states, although cannabis use remains illegal federally. With the increasing prevalence of cannabis use among adults, it is important that anesthesia professionals recognize the potential cardiopulmonary, gastrointestinal, and central nervous system effects of cannabis use when providing perioperative care to those patients who consume cannabis.[2]

PHARMACOLOGICAL CONSIDERATIONS

The cannabis plant contains more than 500 compounds including cannabinoids, terpenoids, and flavonoids.[3] The main cannabinoids are delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD). THC is the major psychoactive component responsible for the properties of sedation, analgesia, and euphoria. Cannabis refers to all products derived from this plant and marijuana refers to the parts of the plant (dried leaves, flowers, stems, and seeds) that contain substantial amounts of THC.[4]

The strength of cannabis is measured by the concentration of THC. The amount of THC in marijuana has been increasing, which may contribute to the increase in emergency room visits.[5] The THC potency in confiscated marijuana samples from the Drug Enforcement Agency has increased from 3% in 1980 to 12% in 2012.[5] The primary reason for the increase in THC strength is a more potent form of cannabis called sinsemilla. Sinsemilla is the female cannabis plant that has not been pollinated and now constitutes the major proportion of seized products.[3,5] Additionally, more marijuana extracts and resins are being produced that contain 3–5 times more THC than the plant itself.[3,5]

The mechanism of action of the cannabinoids is binding and acting as a partial agonist on two types of G-coupled cannabinoid receptors, called cannabinoid receptor type 1 (CB1) and type 2 (CB2).[6,7] The CB1 receptors are

found, in the largest concentrations, in the brain and nervous system tissue, and less in the liver, adipose tissue, and vascular endothelium.[6,7] The CB2 receptors are found predominantly in immune cells such as macrophages and mast cells.[6,7] Activation of CB1 inhibits the release of several neurotransmitters including acetylcholine, L-glutamate, gamma-aminobutyric acid (GABA), norepinephrine, dopamine, and serotonin.[6,7]

Individuals typically intake marijuana through inhalation (smoking or vaporization) or ingestion of an edible product. The pharmacokinetics can be variable depending on the method of administration.[6,7] THC is quickly transferred from the lungs to the bloodstream during smoking, and the onset of psychoactive effects occurs rapidly, within seconds to minutes. The psychoactive effects of THC from inhalation reach a maximum in 15 to 30 minutes and begin to taper off at 2–3 hours. However, the duration of action may be up to four hours. These effects mirror plasma THC concentrations.[6-8] A small amount of inhaled THC, approximately 2 to 3 mg, may produce effects in a naïve user.[8] Pulmonary bioavailability varies from 10 to 35 percent of an inhaled dose and is determined by the depth of inhalation along with the length of time of inhalation and breath-holding.[7,8] Smoking is the most common route of intake, however; vaporization is on the increase.[8,9] Similar psychoactive effects are experienced through vaporization although it may reduce exposure to by-products of combustion.[7-9] However, possibly harmful and carcinogenic aerosols may be present in flavored cannabis vaping products.[10] Orally ingested cannabis has a later onset of action ranging from 60–120 minutes. Cannabis has low bioavailability because of degradation in gastric acid and first-pass metabolism in the liver.[7] The inexperienced user may encounter psychotropic effects with 5 to 20 mg of ingested THC.[8] Orally ingested cannabis reaches its peak effect at approximately 120 minutes and can last up to 4 to 6 hours. The elimination half-life of THC is difficult to measure and is slow, with times ranging from 25 to 36 hours. The slow-release occurs from lipid storage areas and enterohepatic circulation. The elimination half-life increases in regular cannabis users.[7]

THC has high lipophilicity and distributes to highly perfused tissues. It is also highly protein-bound (95 to 99 percent) mainly to lipoproteins and has a volume of distribution of 2.5 to 3.0 L/kg.[7]

Information regarding drug interactions with cannabis is limited as is with many naturally occurring compounds due to the complexity of the plant, variability in the THC content of available products, and lack of studies resulting from difficulty in studying a Schedule I drug. Some information is available through the prescribing information of cannabinoid-derived pharmaceutical medications.[6]

THC is mainly metabolized in the liver through the P450 complex as are many anesthesia drugs, and, therefore, there is a potential for pharmacokinetic drug interactions through either the inhibition or induction of these enzymes (Table 1).[6,7,11] The few cannabis and cannabidiol metabolic drug interactions reported in the literature include increased

Table 1: Pharmacokinetic Drug Interactions With THC and Their Consequences[6,7,11-15]

Increased effects of clobazam, warfarin, hexobarbital.
Decreased effects of theophylline.
Additive pharmacodynamic effects with other agents having similar physiological properties, such as sedation with CNS depressant drugs, including benzodiazepines, opioids, and volatile agents.

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effects of clobazam, warfarin, and hexobarbital, and a decreased effect of theophylline.[12-15] There can also be additive pharmacodynamic effects with other agents having similar physiological properties such as sedation with central nervous system depressant drugs, including benzodiazepines, opioids, and volatile agents.[6,7]

PREOPERATIVE CONSIDERATIONS

There are some important preoperative considerations for patients that are cannabis users. First, it is important to take a good medical history, including the history of cannabis use (Table 2). The anesthesia professional should consider the composition of the products used, a history of adverse effects, the dose consumed, the effects caused by missed doses, and the time since last exposure.[16] Understanding these factors is important in order to assess the risks of cardiovascular and respiratory problems, the potential for withdrawal symptoms (Table 3a), the effects of THC administration on delayed gastric emptying, and the risks associated with anesthesia administration during cannabis intoxication.[16]

The use of cannabis preoperatively may lead to significant safety issues for the patient and health care providers.[1] Preoperatively, it is essential to assess for the signs and symptoms of acute cannabis intoxication, as acute intoxication poses the largest risk to anesthesia administration.[17] Patients with symptoms of acute cannabis intoxication (Table 3b) are more likely to emerge from anesthesia violently.[17] Among cannabis users who have a history of angina, it is important to inquire about angina-free functional capacity during cannabis use.[18] In patients with an elevated risk of coronary artery disease, there is an increased risk of myocardial infarction in the first hour following the use of cannabis, and thus elective surgeries should be delayed by at least one hour following cannabis use in these patients.[18] Preoperative cardiac function tests and cardiology consultation may be required. Cannabis has the potential to inhibit P450 enzymes.[6,11] The patients on anticoagulation and antiplatelet medications should be evaluated for coagulation function. Preoperative lab tests may include PTT, INR, and platelet function tests.

INTRAOPERATIVE CONSIDERATIONS

The current literature is lacking clinical guidance regarding intraoperative anesthesia management in cannabis users. Some research suggests that patients who regularly use cannabis may require larger induction and maintenance doses of anesthesia intraoperatively.[16] Among some patients undergoing sedation for endoscopy procedures, there may be an association between cannabis use and higher intraoperative dose requirements of propofol to achieve adequate sedation, but these claims have not yet been supported by well-designed studies.[19] A recent retrospective study assessing the impact of preoperative cannabis use in patients undergoing open reduction and internal fixation of tibia fractures specifically provided some evidence to suggest minimal effect of preoperative cannabis use on anesthetic dosing intraoperatively.[20] Among the study cohort of 118 patients, of which more than 25% reported cannabis use prior to surgery, there was no significant difference in total propofol, dexmedetomidine, etomidate, ketamine, desflurane, midazolam, and fentanyl doses administered between those who used cannabis prior to surgery and those who did not (patients were classified as cannabis users if they self-reported any cannabis products use in the month prior to surgery, and nonusers if they did not use any cannabis products the month before surgery).[20] The only agent for which there was a significant difference observed between these two groups was sevoflurane, where the average total volume of sevoflurane administered intraoperatively was significantly higher among the group who used cannabis (37.4 ml vs 25 ml, p=0.023).[20] This study suggests that preoperative use of cannabis may lead to increased tolerance to sevoflurane, although the study has some notable limitations including its retrospective study design, and small sample size. Thus, future research is needed to verify these findings.[20]

Anesthesia professionals should take extra caution when using intraoperative sympathomimetics and beta-blockers among those

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Table 2: Perioperative Considerations of Preoperative Cannabis Use on Anesthesia Administration and Postoperative Pain Management[1,2,16-24]

PreOperative Considerations
Assess for signs of cannabis intoxication.
Obtain comprehensive history of product composition, history of adverse effects, dose consumed, the effects caused by missed doses, and the time since last exposure.
Obtain history of angina and increased risk of coronary artery disease.
Evaluate for coagulation dysfunction (e.g., PTT, INR, and platelet function tests).
Consider delaying elective surgeries following acute patient consumption of cannabis
IntraOperative Considerations
Preoperative cannabis use may lead to tolerance to sevoflurane.
Care with intraoperative utilization of sympathomimetics and beta-blockers.
Increased risk of airway hyperactivity.
PostOperative Considerations
More likely to report higher postoperative pain scores and increased analgesic requirements.
Monitor for signs of cannabis withdrawal.

Table 3a: Cannabis Withdrawal Symptoms[16]

Anger	Decreased appetite	Malaise
Irritability	Feelings of depression	Abdominal pain
Nervousness/anxiety	Chills	Sweating
Insomnia	Nightmares	Tremors

Table 3b: Symptoms of acute cannabis intoxication.[17]

Increased anxiety	Paranoia	Psychosis

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using cannabis due to potential inhibition of CYP-450.[16] Furthermore, patients must be carefully monitored intraoperatively for signs of hemodynamic instability and signs of myocardial infarction or stroke. Anesthesia professionals should be prepared to manage airway hyperactivity intraoperatively if the patients do not have a secure airway due to potential airway irritation caused by preoperative cannabis use.[16]

POSTOPERATIVE CONSIDERATIONS

Postoperatively, there are two main considerations for patients who are cannabis users: challenges in the management of postoperative pain, and managing withdrawal symptoms.[16] Several studies have demonstrated that cannabis users are more likely to report higher pain scores, poorer sleep, and require a greater quantity of analgesic medications in the immediate postoperative period than nonusers.[21,22] Therefore, multimodal analgesia and appropriate opioid dosing should be considered for these patients.[16] It is also important to monitor cannabis users for signs and symptoms of withdrawal postoperatively (Table 3a).[23] Withdrawal onset can take place within 1–2 days of the last cannabis use and last 1–2 weeks; thus, health care providers should monitor for signs of cannabis withdrawal in postoperative patients until cannabis use is resumed.[16] Postoperative shivering, hypothermia, and increased platelet aggregation have also been documented among cannabis users.[24] Postoperative hypothermia and shivering is thought to be mediated by CB1 receptor activation and, thus, are not suspected to be due to withdrawal symptoms.[25] Increased platelet aggregation is likely due to CB1 and CB2 receptors existing on platelet membranes by a high dose of THC.[24]

CONCLUSION

The increasing use of cannabis, both medically and recreationally, has resulted in new and important perioperative considerations for anesthesia professionals (Table 2). Having a better understanding of the possible effects of cannabis use perioperatively can help providers mitigate perioperative risk and better manage postoperative pain in patients receiving anesthesia.

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