# Marijuana Use, Vaping, and Preoperative Anesthetic and Surgical Considerations in Clinical Practice

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#### **KEYWORDS**

- Cannabis Perioperative Vaping Cannabinoids Marijuana Anesthesia
- Surgery

#### **KEY POINTS**

- Marijuana, also known as cannabis, is a psychoactive substance derived from the cannabis plant.
- Marijuana and vaping have acquired widespread popularity, with millions of people using them for a variety of reasons, including recreational purposes.
- Marijuana can influence a patient's response to anesthesia, alter postoperative pain management, and increase the risk of complications, whereas vaping can have negative effects on the respiratory system and hinder the body's ability to recover after surgery.
- Vaping is the act of inhalation and exhalation of aerosolized liquid from an electronic cigarette or e-cigarette device.

#### INTRODUCTION

Marijuana, also known as cannabis, is a psychoactive substance derived from the cannabis plant. It has been used for therapeutic and recreational purposes in many cultures throughout history. Recently, its use has increased greatly in many countries.

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In this regard, it is now widely available in legal markets.<sup>1</sup> With increasing legalization of marijuana and increasing consumer access, there is a growing interest in its potential adverse effects, particularly related to smoking and vaping. Vaping is the act of inhalation and exhalation of aerosolized liquid from an electronic cigarette or e-cigarette device.

It has become increasingly popular in recent years as a "safer" alternative for users who may be trying to avoid traditional cigarette smoking<sup>2</sup> and in the adolescent population.<sup>3</sup> Although studies on long-term health effects of vaping are still ongoing, there are some known potential risks associated with using vaporizers for marijuana, such as increased exposure to temperature-induced toxins and other volatile organic compounds that may have damaging effects on the lungs.<sup>4</sup> For patients who have vaped marijuana before surgery, providers should consider many factors when preparing them for their surgical procedure. These may include evaluating the patient's current level of intoxication, exploring the history of marijuana use and its effects on them, assessing pulmonary function for any potential adverse impacts,<sup>5</sup> and determining whether the patient would benefit from nicotine replacement therapy before surgery. It is also important to consider the possibility that a patient could experience withdrawal symptoms or increased anxiety when stopping vaping marijuana in preparation for surgery.<sup>6</sup> Therefore, it is important for clinicians to offer patients preoperative counseling and other support services if needed.

The goal of the present review is to provide an overview of important presurgical and anesthetic considerations for individuals who vape marijuana. By understanding the potential risks associated with vaping marijuana, clinicians can better assess and manage their patients' treatment options and provide appropriate preoperative care. In addition, health care professionals should also consider any comorbidities that may increase the risk or severity of complications during surgery, such as cardiovascular disease or respiratory disorders. Finally, it is important to ensure that any medications prescribed are compatible with the patient's existing medical conditions before undergoing surgery. When providing education regarding risks associated with vaping marijuana before surgery, health care providers should emphasize the importance of following all postoperative instructions to avoid any unnecessary complications during recovery. With a comprehensive approach to preoperative care and patient safety, health care professionals can ensure a successful outcome for individuals who have vaped marijuana before undergoing surgical procedures while promoting the importance of responsible use of marijuana and vaping devices.

## CANNABIS PHARMACOKINETICS AND PHARMACODYNAMICS Pharmacokinetics

Cannabis contains more than 100 different compounds, including cannabinoids, terpenes, and flavonoids.<sup>7,8</sup> The most well-known and studied of these compounds are delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD). THC is the primary psychoactive compound of cannabis, whereas CBD has been proven to have a wide range of actions without causing psychoactive effects.<sup>9–11</sup>

#### Absorption

When cannabis is smoked, THC is immediately absorbed into blood through the lungs and achieves peak levels within minutes.<sup>12</sup> When cannabis is ingested, such as in edibles, the onset of effects is slower, and peak levels are reached after several hours. This is related to the fact that THC is first metabolized by the liver into its active form, 11-hydroxy-THC.<sup>13</sup>

## Distribution

The distribution of THC in the body is also complex. THC is highly lipophilic, which leads to high volume of distribution, or the amount of drug that is distributed throughout the body.<sup>14</sup> THC is also highly protein-bound, binding to proteins in blood and is not easily filtered by the kidneys, thus prolonging its half-life.

#### Metabolism

The metabolism of THC is primarily carried out by the cytochromes P450 (CYP 450) system in the liver, where it is broken down into several metabolites, including 11-hy-droxy-THC and THC-carboxy group (COOH). These metabolites undergo glucuronidation<sup>15</sup> and are then excreted in the urine and feces.

#### Elimination

The elimination half-life of THC can vary widely, ranging from several hours to several days, depending on factors such as the dose, frequency of use, and individual metabolism. Most studies have found that metabolites of THC have a long half-life of up to 4 days owing to their release of THC from lipid-storage compartments and significant enterohepatic circulation.<sup>16</sup>

The metabolites and elimination profile of CBD have been less extensively studied as compared with THC. Most studies that have specifically examined the pharmacokinetic profile of Epidiolex, an oral formulation of CBD used in the treatment of epilepsy, indicate that following single administration, CBD reaches peak concentration in around 4 hours. CBD is also highly lipophilic, readily crosses the blood-brain barrier and has a large volume of distribution. It undergoes metabolism by CYP 450 system into 7-OH-CBD that is subsequently converted into the 7-COOH-CBD. These metabolites undergo glucuronidation in the liver and are excreted over the course of several days.<sup>17</sup>

#### Pharmacodynamics

When administered via smoking or vaporization, the active constituents of cannabis enter the body in the form of aerosolized particles, which quickly reach the lungs, wherein they diffuse into the circulation. Once absorbed, various compounds within marijuana (eq. THC, CBD) interact with endocannabinoid receptors cannabinoid receptor (CB)1 and CB2 to produce both desired therapeutic effects as well as adverse reactions. Extensive studies in the 1990s led to the discovery of CB1 and CB2 receptors, a class of G-protein-coupled receptors.<sup>18</sup> CB1 receptors are predominantly found in the brain, mainly in the substantia nigra, the basal ganglia, the limbic system, the hippocampus, and cerebellum, but are also expressed in the peripheral nervous system, liver, thyroid, uterus, bones, and testicular tissue. CB1Rs are found at the terminals of central and peripheral neurons, where they mostly mediate inhibitory action on the ongoing release of a number of excitatory and inhibitory dopaminergic, gamma-aminobutyric acid (GABA), glutamatergic, serotoninergic, noradrenalin, and acetylcholine neurotransmitter systems, affecting functions such as cognition, memory, motor movements, and pain perception.<sup>10</sup> CB2Rs are found in immune cells, the spleen, and the gastrointestinal system.<sup>19,20</sup> THC acts as a partial agonist at cannabinoid 1 receptor (CB1R). Many research studies suggest that rather than a direct effect, CBD potentiates the pharmacologic effects of d-9-THC via a CB1R-dependent mechanism.9

In addition to these direct effects on cannabinoid receptors, nicotine found in many vaping products produces additional direct effects on nicotinic acetylcholine

receptors, resulting in increased risk for adverse incidents, including nicotine-induced anxiety and agitation.  $^{\mbox{21}}$ 

## CANNABIS PHYSIOLOGIC EFFECTS Pain Relief Associated with Cannabis

Cannabis has been shown to have analgesic properties and has been used for the treatment of chronic pain. THC and other cannabinoids interact with the endocannabinoid system (ECS) to modulate pain sensation through multiple mechanisms, including activation of CB1 receptors in the brain and spinal cord, inhibition of inflammatory mediators, and modulation of the release of neurotransmitters involved in pain processing.<sup>22–24</sup>

## Appetite Stimulation

Cannabis can stimulate appetite, an effect that has been attributed to the activation of CB1 receptors in the brain. THC has been shown to increase the release of the appetite-stimulating hormone ghrelin and reduce the release of the satiety hormone leptin, leading to an increase in food intake.<sup>25,26</sup>

## Epilepsy

CBD has been shown to have neuroprotective, anticonvulsant, anxiolytic, antipsychotic, and anti-inflammatory properties. A multicenter randomized controlled trial demonstrated seizure reduction of up to 41%<sup>27</sup> in patients with rare epilepsy disorders such as Dravet and Lennox–Gastaut syndromes. In 2018, US Food and Drug Administration (FDA) approved use of Epidiolex, plant-derived, purified pharmaceuticalgrade CBD medication for treatment of patients more than 2 years of age in these rare seizure disorders.<sup>28</sup>

## Mood Alteration

Multiple studies have demonstrated that THC and CBD have opposite effects on the brain. Although THC is found to induce anxiety and psychotic symptoms and cause memory impairment, CBD is found to have anxiolytic, antipsychotic properties, and it does not impair memory and cognitive functions.<sup>29</sup> This has led to research exploring the utility of CBD for mood disorders<sup>30</sup> and psychotic disorders like schizo-phrenia through action on a different set of receptors than CB1R.<sup>29,31,32</sup>

## Memory Impairment

Cannabis use has been associated with memory impairment, particularly in the short term. THC has been shown to impair working memory and attention through the modulation of the prefrontal cortex, a brain region critical for these cognitive processes. In a clinical trial on healthy subjects who did not consume cannabis, administering delta-9-THC led to impaired verbal recall along with other psychotic symptoms.<sup>33</sup>

## **Cardiovascular Effects**

Cannabis use can lead to cardiovascular effects, including an increase in heart rate, blood pressure, and myocardial oxygen demand.<sup>34</sup> These effects are thought to be due to the activation of CB1 receptors in the heart and blood vessels<sup>35,36</sup> and the release of stress hormones. These effects can be particularly concerning in the perioperative period, as they can increase the risk of perioperative cardiovascular events, such as myocardial infarction and stroke. It is important at the time of preoperative assessment for the anesthesiologist to screen patients for cardiovascular risk factors and to consider delaying surgery in patients with significant cardiovascular disease.

#### **Respiratory Effects**

Cannabis smoke contains a range of toxicants and carcinogens, and smoking cannabis was found to cause hyperinflation and increase in large airway resistance, without evidence of airflow obstruction or impairment of gas transfer; those effects are different from the effects of tobacco smoking<sup>37</sup> and can lead to respiratory effects, including bronchitis, chronic cough, and impaired lung function.<sup>38</sup> These effects can be particularly concerning in the perioperative period, as they can increase the risk of perioperative respiratory complications, such as atelectasis and pneumonia. Patients who smoke cannabis should be counseled to stop smoking before surgery and to use alternative methods of administration, such as vaporization or ingestion.

#### Clinical Considerations in Patients Vaping Marijuana in the Preoperative Period

Vaping is becoming increasingly popular as a method of delivery for marijuana, especially in adolescents, but there are limited data regarding its safety profile, especially in the preoperative period. Vaping refers to the vaporization of substances such as flavors, nicotine, or cannabis products, whereby liquid, oil, or plant material are heated to a temperature that releases an aerosolized mixture of water vapor and active ingredients (eg, nicotine in e-cigs and THC or CBD for cannabis), which is then inhaled.<sup>39,40</sup> This method of administration avoids combustion of the substance and the inhaling of smoke, which contains carbon monoxide and other by-products of combustion, thereby minimizing some respiratory effects associated with smoking marijuana, such as increased bronchial reactivity and lung inflammation.<sup>41</sup>

Smoking and vaping cannabis produce similar bioavailability profiles with respect to delta-9 THC levels. However, related to differences in inhalation technique and device technology, studies suggest that vaping may be associated with higher concentrations of THC in the blood.<sup>42</sup> It has also been suggested that smoking and vaping can produce similar levels of carbon monoxide, though this is still unconfirmed. The pharmacokinetics of vaping marijuana also differs significantly from smoking or ingesting it orally. Vaping marijuana yields a more rapid onset of action in comparison with other methods related to increased bioavailability through rapid absorption in the lungs, meaning that there is less time before effects are experienced.<sup>43</sup> This means that clinicians should be aware of potential decreased reaction time and impaired judgment in these patients that can be associated with marijuana use.

Given these potential differences in pharmacokinetics, it is important to consider potential presurgical and preanesthetic implications for patients who vape marijuana before undergoing surgery. In addition to assessing potential drug interactions, patients should also disclose whether they have vaped marijuana within 24 hours before surgery. This information is important for preanesthetic assessment, so that anesthesia can be tailored based on the pharmacokinetic properties of cannabis and its metabolites. The use of e-cigarettes per se is associated with bronchial hyperreactivity, reduced ciliary function, and impaired cough, which may lead to increased respiratory complications.<sup>44–46</sup> Furthermore, related to prolonged elimination times associated with vaping cannabis compared with smoking, particular attention should be paid when deciding if and when a patient should receive procedural sedation or general anesthesia.

Clinicians must consider the possibility that a patient may still have cannabis in their system and its effects on the body, even if they have not used it recently. Cannabis can influence pain perception, motor coordination, cognition, and alertness, which are all factors that need to be considered when assessing a patient's fitness for surgery.<sup>47</sup> Health care providers should consider the psychoactive properties of cannabis

when formulating preoperative plans so that they can adequately prepare patients who may become acutely intoxicated after vaporizing or smoking marijuana products.

Finally, during the presurgical/preanesthetic evaluation, it is also important to note that most states have adopted laws allowing for medical or recreational cannabis use, so clinicians need to consider the legal implications when working with patients who vape marijuana. The rules and regulations governing cannabis use vary greatly by state, so it is essential to be aware of those regulations when providing care.<sup>48</sup>

# INTRAOPERATIVE ANESTHESIA CONSIDERATIONS Drug Interactions

Cannabis use can interact with other medications, including anesthetic agents and analgesics. E-liquids containing cannabinoids are likely to have similar anesthetic implications to cannabinoids ingested by other routes. Cannabinoids will compete for CYP3A4 and CYP2C9 enzymes, resulting in a possible decrease in the metabolism of other substrates.<sup>49</sup> They can interact with the GABAergic system, which is critical for the activity of many anesthetic agents. A prospective trial on a small group of patients determined that the required dose of propofol to facilitate laryngeal mask insertion was higher in patients consuming cannabis.<sup>50</sup> Health care providers should be aware of potential drug interactions and should screen patients for cannabis use before surgery. Both cannabis and tobacco consumption induce CYP1A2, and when smoked together, the induction is additive.<sup>51</sup> This may be significant for patients who are also being administered a CYP1A2-metabolized drug.

## Pain Management

Multiple preclinical studies have revealed that cannabinoid and opioid receptors have similar signal transduction systems along pain pathways, displaying an opioid-sparing effect.<sup>52,53</sup> Cannabis has been shown to have analgesic properties and has been used for the treatment of chronic pain. In contrast, prolonged cannabis use can also lead to tolerance and withdrawal, and studies have demonstrated increased opioid use in the postoperative period.<sup>54</sup> Anesthesiologists and surgeons should be aware of patients' cannabis use history and should consider alternative pain management strategies in patients with a history of chronic cannabis use.

## Postoperative Nausea and Vomiting

Postoperative nausea and vomiting (PONV) is a common complication of anesthesia and surgery, and it can lead to prolonged hospital stays and patient discomfort. Although initial studies have explored the role of cannabinoids as an effective antiemetic in patients with cancer, recent studies have demonstrated that the prolonged use of cannabis is associated with hyperemesis, and the best way to prevent it is abstinence before surgery.<sup>55,56</sup>

## Cannabis Withdrawal Syndrome

Cannabis withdrawal syndrome (CWS) is a clinical syndrome that can occur in patients who use cannabis chronically and then stop or reduce their use. The syndrome is characterized by symptoms such as irritability, insomnia, decreased appetite, and anxiety, probably secondary to CB1R downregulation.<sup>57</sup> At present, there are no drugs approved for the treatment of CWS in the perioperative period, but zolpidem and mirtazapine have been shown to help with some of the symptoms associated with CWS.<sup>58</sup>

#### **RECENT CLINICAL FINDINGS**

Given recent legalization in multiple states and increased research to explore the use of marijuana for medical indications such as treatment of opioid withdrawal and epilepsy, the number of cannabis users presenting for elective surgeries has steadily increased. A recent study done at an academic center in Boston observed that every seventh patient presenting for elective surgery was a cannabis user.<sup>59</sup> Hence, continuous efforts have been made to establish guidelines for the safe anesthetic management of these patients.

One of the first guidelines for perioperative management of cannabis users was presented by the Perioperative Pain and Addiction Interdisciplinary Network. These guidelines made recommendations to define significant cannabis consumption<sup>60</sup> and recommended weaning cannabis more than 7 days before surgery in patients consuming more than 1.5 g/day of smoked cannabis, 300 mg/day of CBD oil, and 20 mg/day THC oil. These guidelines also emphasized the need of providing additional PONV prophylaxis and the use of additional anesthetic agents to maintain adequate depth intraoperatively. Similarly, Anesthesia Patient Safety Guidelines provide recommendations emphasizing thorough preoperative assessment and intraoperative monitoring for signs of hemodynamic instability, stroke, and airway emergencies secondary to hyperreactive airway.<sup>61</sup>

The American Society of Regional Anesthesia also published detailed guidelines to assist physicians in decision-making in evaluating patients with chronic cannabis use especially in special population groups like pregnant patients before surgery.<sup>62</sup> These guidelines reiterate that patients with history of cannabis use should be screened and postponing surgery should be considered in patients with signs of intoxication. A procedure should be delayed for at least 2 hours after the last cannabis inhalation.

#### SUMMARY

The pharmacodynamics of marijuana and vaping are complex, and health care providers must remain informed about the latest research to ensure a safe and effective anesthetic experience for patients who have vaped marijuana products. The importance of patient education cannot be overstated, as it can help to minimize any potential adverse effects associated with the combined use of both marijuana products and anesthesia medications during surgical treatments. Furthermore, continuous monitoring of patients throughout the entire procedure should be conducted to ensure that any adverse reactions are quickly addressed. In summary, consideration of the pharmacodynamics of marijuana use, and vaping, focused presurgical/preanesthetic evaluation and adherence to standard guidelines are essential steps for anesthesiologists and surgeons to take when treating patients who have vaped or smoked marijuana before undergoing a surgical procedure.

## **CLINICS CARE POINTS**

- The importance of patient education cannot be overstated, as it can help to minimize any potential adverse effects associated with the combined use of both marijuana products and anesthesia medications.
- Continuous monitoring of patients throughout the entire procedure should be conducted to ensure that any adverse reactions are quickly addressed.

## **CONFLICTS OF INTEREST**

None.

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