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The impact of cannabis use on local anesthetic dosing during hair restoration surgery: a case report, proposed mechanisms, and clinical recommendations

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ABSTRACT

Cannabis use has increased significantly in the last decade. This article presents a case where a patient needed more local anesthetic (LA) than usual to induce effective anesthesia during hair transplant surgery. The reason cannabis users often need more LA is poorly understood. One possibility is that cannabis withdrawal effect makes patients more sensitive to pain and stress. Additionally, vasodilatory property of cannabis may speed up LA clearance from the application site. The interactions of two major cannabinoids, cannabidiol (CBD) and tetrahydrocannabinol (THC), with cannabinoid receptor type 1 (CB1), cannabinoid receptor type 2 (CB2), and transient receptor potential vanilloid 1 (TRPV1) receptors are also complex. Furthermore, CBD and THC function as cytochrome P450 enzyme inhibitors potentially impacting systemic metabolism. When planning to administer LA during hair restoration surgery in cannabis users, clinicians should obtain a detailed history of prior consumption (type of cannabis, frequency, dosage). Preoperative planning should consider the anticipated duration of surgery and calculate the maximum safe LA dose to avoid the risk of toxicity. Also, patients should be carefully monitored for vital signs during surgery. If a patient requires frequent re-injection to remain pain free, the surgeon may need to re-assess the surgical plan to avoid toxicity.

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KEYWORDS
Cannabis; cannbinoids; local anesthetics; hair transplant surgery

1. Introduction

Over the past ten years, cannabis usage has surged, primarily because it has been legalized for both medical and recreational use in several countries around the world (1). Although cannabis has demonstrated a few therapeutic benefits, its use presents specific challenges in clinical settings, especially during surgical procedures that involve local anesthesia. Cannabis users frequently show changes in pain sensitivity and increased resistance to typical doses of local anesthetics, which complicates effective anesthesia management (2).

A number of case reports have indicated that cannabis users often need increased doses of local anesthetics to achieve adequate pain relief during medical, hair transplant or dental procedures. The mechanisms behind this altered response are still not well understood or extensively researched.

This article comprehensively overviews the connection between cannabis use and the changes in local anesthetic requirements, particularly during hair restoration surgery. We present a case report, review clinical studies, and explore possible mechanisms in order to improve understanding and aid clinicians in optimizing perioperative care for cannabis users. In addition, the article will detail practical considerations for managing anesthesia before, during, and after surgical procedures to ensure both patient safety and effective pain control.

2. Case report

2.1. Patient information

A 51-year-old male presented for hair transplant surgery involving the follicular unit excision (FUE) method, requiring 1000 grafts. He had a history of four previous hair restoration procedures at the same office: three utilizing the follicular unit transplantation (FUT) method and one prior FUE procedure. Although his medical history was reportedly negative for drug or alcohol use, the patient later disclosed that he was a long term cannabis user. At the time of the procedure, the patient was using finasteride (½ tablet on Mondays, Wednesdays, and Fridays) and had recently initiated testosterone cypionate therapy for low testosterone. Records of prior local anesthetic use during previous surgeries were unavailable; however, neither the patient nor the clinician recalled any prior tolerance to local anesthesia.

2.2. Clinical context

The chosen anesthetic protocol involved the use of 1% lidocaine mixed with 0.25% bupivacaine (Marcaine) in a 1:1 ratio, combined with 1:100,000 epinephrine, totaling 10 cc per syringe. Additionally, preoperative sedation included 20 mg of diazepam, which had minimal sedative effect.

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2.3. Event description

During the procedure, the patient exhibited an unusual hyperalgesic response to local anesthetic administration, characterized by wincing, jaw clenching, and pronounced complaints of pain during the injections. This reaction was inconsistent with typical patient responses and with the patient's own experiences during previous surgeries. Standard measures to minimize discomfort, including vibration application, slow injection (3–4 ml/min), and use of a 27 G needle, were employed but were only partially effective. The solution was not buffered.

An initial 20 cc of local anesthetic achieved sufficient donor area anesthesia, but the patient required repeat injections to maintain analgesia throughout the procedure, which was atypical given the relatively short duration of the FUE harvesting process. Despite efforts to maintain comfort, the patient experienced persistent donor area pain and required additional anesthetic supplementation. An occipital nerve block provided limited relief, and recipient area anesthesia was similarly challenging to sustain.

The following morning, the patient returned for a postoperative visit, reporting nausea and emesis, which were successfully treated with 8 mg of ondansetron. It was during a follow-up visit one week later, the patient disclosed daily cannabis vaping ("canary yellow" cannabis, typically one hit in the morning and one at night) for several years. He also revealed a two-day cessation of cannabis use prior to surgery, suggesting the possibility of cannabis withdrawal as a contributing factor to his symptoms and heightened pain sensitivity.

2.4. Diagnostic workup

Routine preoperative laboratory evaluations, including a complete blood count (CBC) and comprehensive metabolic panel (CMP), were normal. No additional diagnostic tests were performed.

2.5. Management

The patient needed a higher dose of local anesthetic; however, the total amount administered was kept within safe limits. As it became increasingly challenging to maintain anesthesia, 2 amps of 4% articaine with epinephrine were administered, as the mechanism of metabolism was different, and this agent proved to be more effective. However, its use was also cautiously limited due to the potential risk of methemoglobinemia.

2.6. Discussion

This case highlights how prolonged cannabis use can impact the effectiveness of local anesthetics and modify pain sensitivity during surgical procedures. The patient's frequent requirement for additional anesthetic during the procedure indicate an altered pain threshold, which may have been exacerbated by cannabis withdrawal. His hyperalgesic response was also atypical. The authors assume that modifying anesthetic protocols by incorporating stronger agents or buffering solutions may improve outcomes in similar situations.

3. Studies and case reports from the literature: local anesthetics

A pilot study has been published which aimed to evaluate the efficacy of local anesthetics in dental patients who were chronic cannabis users compared to nonusers (2). The study involved 35 healthy adults, where participants received a standard maxillary infiltration of 2% lidocaine with 1:100,000 epinephrine (2). The results indicated that 88% of nonusers (15/17) and 61% of users (11/18) achieved successful anesthesia, defined as onset within 10 min and lasting at least 15 min (2). Since the difference was not statistically significant ($p = 0.073$), the study concluded that there were no significant differences in anesthetic success, onset, or duration between the two groups (2). The authors concluded that larger studies are necessary to confirm these findings due to the limited sample size and variability in cannabis use patterns among participants (2). However, even if this study had involved a more significant sample size, it did not address the issue of faster metabolism or diminished duration of efficacy locally, which is important in the case of hair restoration surgery, which typically requires several hours of local anesthetic effect.

Dental professionals have noted that patients who use cannabis might require more local anesthetic due to the effects of THC on the central nervous system reportedly similar to heightened pain sensitivity encountered with long term opiate use (3). Increased dose of local anesthetic can lead to increased heart rates and potential cardiac complications when local anesthetics containing epinephrine are administered (3).

4. Studies and case reports from the literature: general anesthetics

A case report detailed a 37-year-old male patient with a history of regular cannabis consumption who required large doses of propofol, thiopental, and sevoflurane for anesthesia during an arthroscopic shoulder stabilization (4). The patient's history of cannabis intake was considered a factor in the increased anesthetic requirements (4).

An observational study investigated postoperative shivering among cannabis users, finding that these individuals experienced shivering more frequently than nonusers (5,6). The study monitored core body temperature during surgery and suggested that chronic cannabis use could influence anesthetic depth and recovery (5,6).

5. Mechanism of action

In clinical settings, clinicians have observed that cannabis users frequently require higher doses of local anesthetics to achieve effective anesthesia. A study found that individuals using cannabis daily had significantly reduced pain tolerance compared to non-users, with median cold pressor test (CPT) times of 46 s versus 105 s for controls (7). However, the molecular mechanisms underlying this phenomenon are still not well understood. Furthermore, it remains unclear whether the need for higher doses of local anesthetics is due to cannabis use itself or the effects of withdrawal.

Cannabis contains a variety of cannabinoids that interact with receptors in different ways. We examined several hypotheses to elucidate the potential mechanisms that may account for the increased local anesthetic requirements in cannabis users. However, understanding which pathways play a dominant role in producing the net effect is complex and varies based on an individual patient's physiological differences (Figure 1).

5.1. Cannabis withdrawal effects

Cannabis withdrawal syndrome can arise after the sudden cessation or substantial reduction of cannabis use pre-operatively,

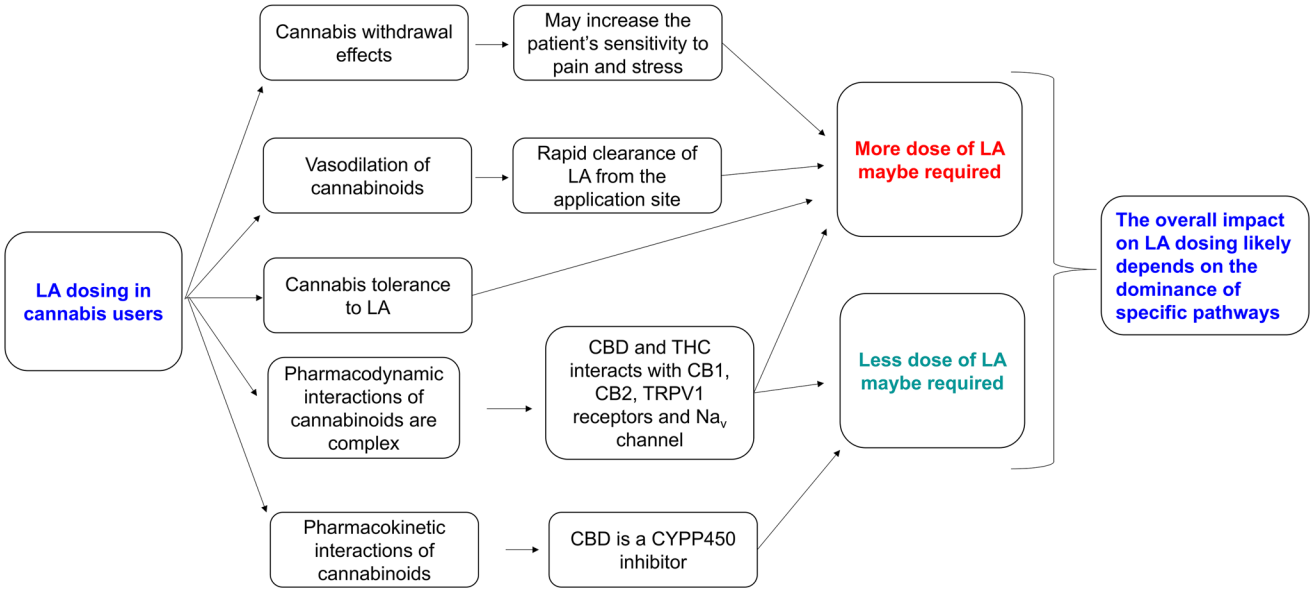


Figure 1. Potential mechanisms by which cannabinoids may affect local anesthetic dosing during surgery.
CB1: Cannabinoid receptor type 1; CB2: cannabinoid receptor type 2; CBD: Cannabidiol; LA: Local anesthetics; THC: Tetrahydrocannabinol; TRPV1: Transient receptor potential vanilloid 1; Na$_v$: Voltage-gated sodium channel

especially in regular or heavy users. Common symptoms include irritability, anxiety, depressed mood, insomnia, loss of appetite, headaches, abdominal pain, and tremors. Additionally, individuals using cannabis for pain management may experience heightened pain levels during withdrawal (8).

The withdrawal symptoms of cannabis typically begin within 24 to 48 h after stopping cannabis use, peak around days 2 to 6, and may persist for several weeks (8,9). Cannabis withdrawal during surgery may contribute to an increased requirement for local anesthetics to achieve effective anesthesia, as the withdrawal state may increase the patient's sensitivity to pain and stress (Figure 1).

5.2. Vasodilatory effect of cannabis

Cannabinoids, including THC, primarily induce vasodilation by activating cannabinoid receptors (cannabinoid receptor type 1 (CB1) and cannabinoid receptor type 2 (CB2)) and other pathways, such as transient receptor potential vanilloid 1 (TRPV1) receptors (Figure 2) (10,11). This peripheral vasodilation may theoretically reduce lidocaine's effectiveness by increasing blood flow, which could lead to its faster clearance from the site of action. However, when lidocaine is combined with epinephrine, a common additive in lidocaine formulations, this effect can be counteracted.

5.3. Cannabis tolerance

Regular cannabis users may develop a tolerance to various substances, including anesthetics. This tolerance can lead to the need for higher doses to achieve the same level of sedation or analgesia compared to non-users (Figure 1). Studies have indicated that daily or weekly cannabis users might require significantly more anesthetic agents, such as propofol, to achieve adequate sedation—sometimes up to three times more than non-users (12).

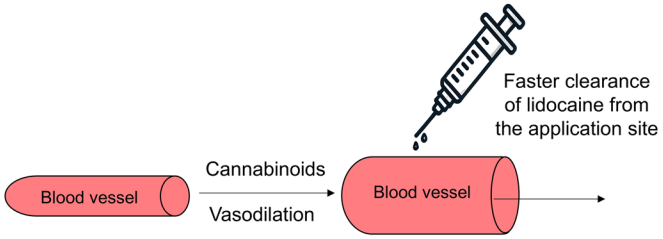


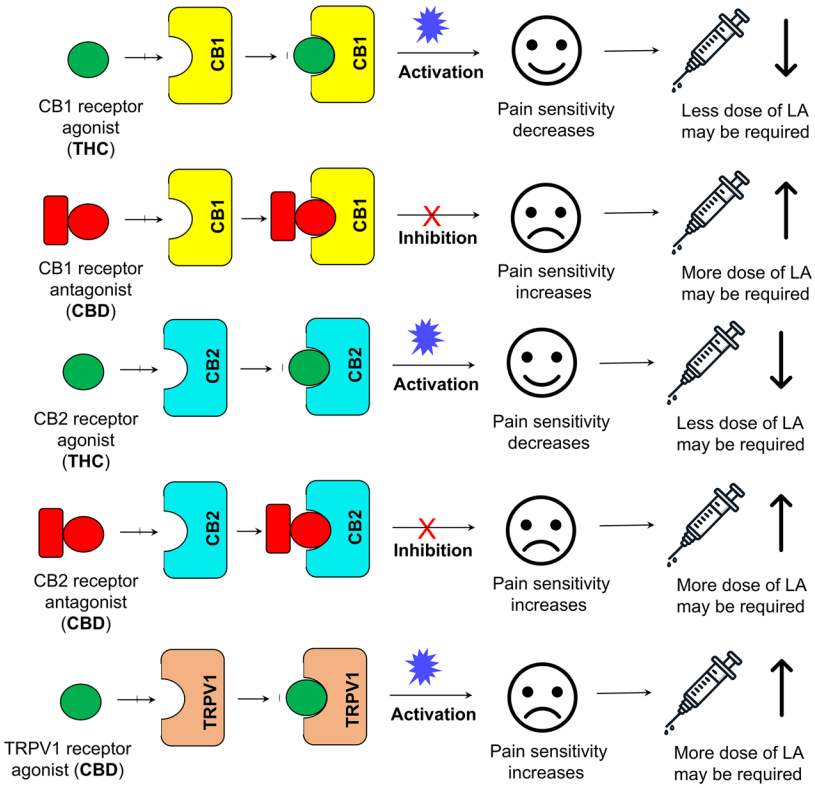
Figure 2. Cannabinoids may act as vasodilators, potentially leading to the faster clearance of local anesthetics from their site of action.

5.4. Effect of CBD and THC on CB1, CB2 and TRPV1 receptors

Cannabis contains various cannabinoids that interact with the body's endocannabinoid system (13). Both CBD and THC interact with CB1, CB2, and TRPV1 receptors (Figure 3). CBD functions as a negative allosteric modulator of CB1, an antagonist of CB2, and an agonist of TRPV1 receptors, leading to increased pain sensitivity (13–16). Consequently, higher doses of local anesthetics may be required to induce sufficient anesthesia. In contrast, THC acts as a partial agonist of CB1 and CB2 receptors, potentially reducing the required dose of local anesthetics (13,17). The overall effect of cannabis on local anesthetic dosage depends on the dominance of receptor activity and individual variability.

5.5. Cannabinoids function as cytochrome p450 enzyme inhibitors

Cannabinoids like CBD and THC predominantly function as inhibitors of cytochrome P450 enzymes (18). A popular local anesthetic such as lidocaine is primarily metabolized in the liver *via* cytochrome P450 enzymes, particularly CYP3A4 and CYP2C9 (18). Cannabinoids, particularly CBD, can inhibit these enzymes, potentially reducing the systemic metabolism of lidocaine. This may



Receptor activity	CBD	THC
CB1 activity	Negative allosteric modulator	Partial agonist
CB2 activity	Antagonist	Partial agonist
TRPV1 activity	Agonist	Not specified

Figure 3. Cannabinoids may alter the dose requirements of local anesthetics. CBD acts as a negative allosteric modulator of the CB1 receptor, an antagonist to the CB2 receptor, and an agonist of the TRPV1 receptor. These interactions of CBD may result in the need for higher doses of local anesthetics in cannabis users during surgery. THC, on the other hand, acts as a partial agonist of both CB1 and CB2 receptors, potentially reducing the required dose of local anesthetics in cannabis users. The net effect on local anesthetic dosing likely depends on which pathways dominate.
CB1: Cannabinoid receptor type 1; CB2: cannabinoid receptor type 2; CBD: Cannabidiol; LA: Local anesthetics; THC: Tetrahydrocannabinol; TRPV1: Transient receptor potential vanilloid 1

result in elevated plasma levels of lidocaine and prolonged systemic anesthetic effects increasing the risk for toxicity (19).

5.6. Dual action of lidocaine

Lidocaine's primary mechanism as a local anesthetic involves blocking voltage-gated sodium channels at the inactivated stage, leading to a reversible inhibition of action potential propagation in neurons (20) (Figure 4). On the other hand, in cell culture models, lidocaine directly activated TRPV1 channels in a concentration-dependent manner, resulting in the release of calcitonin gene-related peptide (CGRP), a neuropeptide involved in neurogenic inflammation (21,22). Thus, lidocaine may have a dual role—it acts as a local anesthetic and may contribute to inflammatory processes *via* the TRPV1 pathway, particularly at higher concentrations.

5.7. Effect of CBD on voltage-gated sodium channel (Na_v)

CBD may inhibit peak sodium currents in a concentration-dependent manner across various Na_v channel subtypes, including $Na_v1.1$, $Na_v1.2$, $Na_v1.6$, thereby reducing excitability and action potential frequency in neurons (23,24).

6. Considerations for using local anesthetics in cannabis users

6.1. Preoperative considerations

6.1.1. Communication with patients

Patients should be encouraged to openly disclose their cannabis consumption with their healthcare providers (25). It is important to obtain detailed history of cannabis use including the type of cannabis consumption (concentration of THC/CBD) and frequency of use in order to help predict the risk of withdrawal symptoms and possible tolerance to medication.

6.1.2. Evaluation of cardiovascular risks

Studies indicate that cannabis use can exacerbate cardiovascular risks (Figure 5), particularly in cannabis-naive individuals (26). For instance, individuals with stable angina who smoke tobacco have been found to develop angina symptoms more quickly after using cannabis. Moreover, research has demonstrated that the risk of myocardial infarction (MI) increases fivefold within the first hour of cannabis consumption, whereas cocaine use is associated with a 24-fold increase in MI risk during the same period (26). This elevated risk is primarily attributed to the combined effects of increased heart rate, peripheral vasodilation, compensatory orthostatic hypotension, and heightened cardiac workload (26,27). However, the risk tends to diminish after one hour, and regular cannabis users may develop partial physiological tolerance to these cardiovascular effects.

Given these cardiovascular implications, it is crucial to assess a patient's cardiac history before administering local anesthesia, especially in those with preexisting heart conditions (6,26). Particular caution should be taken when using local anesthetics containing epinephrine, as they may further amplify cannabis-induced cardiovascular effects.

6.1.3. Monitoring for acute intoxication

Clinicians or anesthesiologists should be vigilant for signs of acute cannabis intoxication, which can impair memory and perception, potentially affecting informed consent (26). In cases of intoxication,

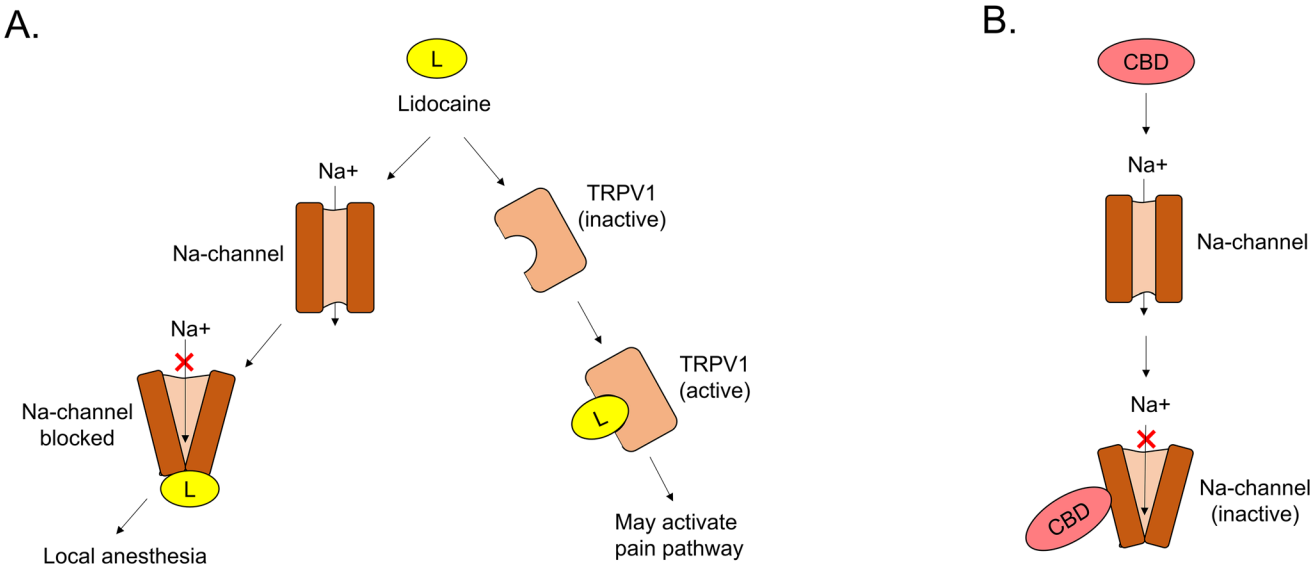


Figure 4. (A) Lidocaine binds to voltage-gated Na + channels in their inactivated state (on the interior side), blocking voltage-dependent Na + conductance and preventing depolarization. This inhibition disrupts the initiation and propagation of action potentials, thereby producing local anesthesia. Conversely, lidocaine may also activate the pain pathway through the TRPV1 channel, particularly at higher concentration. (B) CBD can inhibit peak sodium currents in a concentration-dependent way, leading to decreased neuronal excitability and reduced action potential frequency. Consequently, a lower dose of LA may be needed. However, the overall effect of CBD on LA dosing ultimately depends on which pathways exert dominant influence (Figure 1).
L: Lidocaine; CBD: Cannabidiol; TRPV1: Transient receptor potential vanilloid 1; LA: Local anesthetic

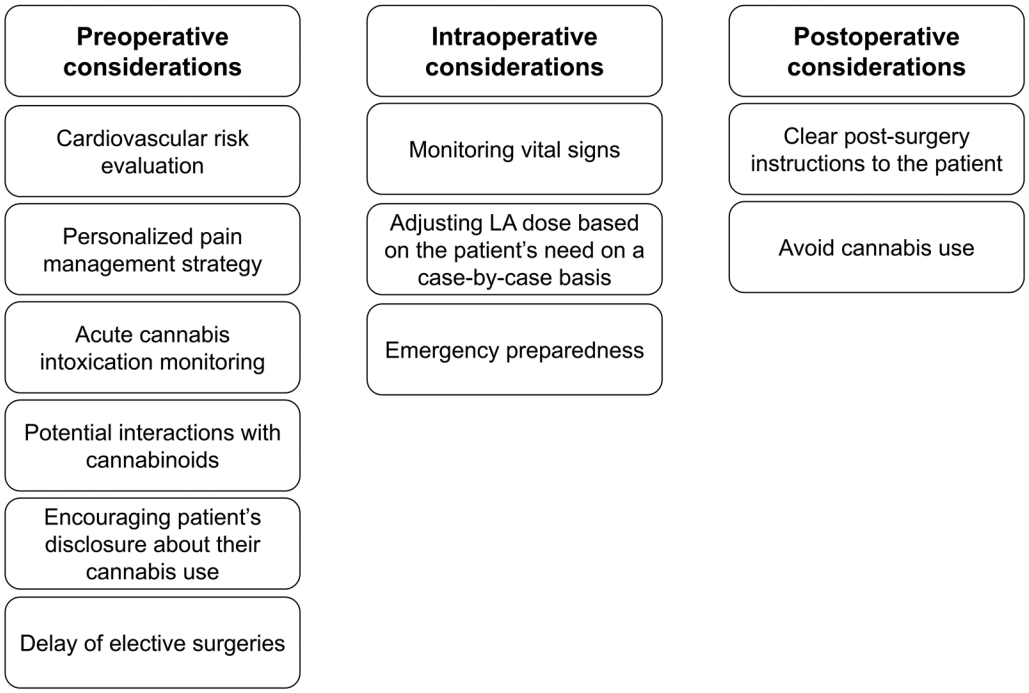


Figure 5. Preoperative, intraoperative, and postoperative considerations for using local anesthetics in cannabis users during surgery (6,13,25–29).

it may be necessary to postpone medically necessary procedures until the patient is sober. In the case of hair restoration surgery, which is cosmetic and elective, eliminating associated risks of withdrawal during and after surgery may be best mitigated by withdrawing cannabis several weeks prior to surgery.

6.1.4. Pain management

Cannabis users may experience altered pain thresholds, necessitating personalized approaches to pain management. Additionally, preprocedure anxiety may be elevated in cannabis users, so it is advisable to offer reassurance or discuss the use of mild anxiolytics, if appropriate.

6.1.5. Potential interactions of cannbinoids

Cannabinoids can interact with a range of medications, including anesthetics and analgesics. Physicians should be mindful of these interactions and adjust dosages as necessary.

6.1.6. Delay of surgeries

If a patient has recently used cannabis, it may be wise to delay elective surgery for 2 to 4 weeks to avoid any cannabis withdrawal symptoms. For medically necessary surgery, clinicians may consider delaying at least an hour after consumption to minimize the risk of complications, such as myocardial

infarction (MI), and to allow time for the acute effects to diminish.

6.2. Monitoring during surgery

Patients may not disclose cannabis use preoperatively, or may not discontinue using it despite medical advice to do so. Therefore, vital signs, especially blood pressure and heart rate, should be closely monitored in cannabis users due to the risk of autonomic instability (28). Additionally, healthcare providers should remain alert for signs of exaggerated responses or adverse effects, such as dizziness, palpitations, or changes in mental status.

6.2.1. Monitoring for lidocaine toxicity during the surgical procedure

It is important to keep an account of the total dose of anesthetic administered during surgery, especially if the patient is still in pain and requires additional anesthetic. For example, during a hair transplant lasting 8–10 h, the maximal recommended total daily lidocaine dosage (with epinephrine) is 500 mg (7 mg/kg/day) (29). There is an ongoing dynamic interaction resulting from metabolism of the lidocaine with a corresponding decrease in serum levels; however, there may be a sequestration of lidocaine in tissues such as cardiac tissue, with the possibility of the total lidocaine dosage exceeding safe levels.

6.2.2. Emergency preparedness

It is vital to have resuscitative equipment readily accessible during surgery, as individuals who are heavy users of cannabis may exhibit unpredictable responses to stress or medications. Preparedness is key to effectively managing potential complications, including vasovagal syncope, heightened anxiety, and cardiovascular instability.

6.3. Post-procedural care

Clear post-procedural instructions should be given, emphasizing the potential interactions between cannabis and prescribed pain medications (26). Patients should be advised to refrain from using cannabis immediately after procedures, as it may, in some instances, increase the risk of bleeding or hinder healing by delaying clotting or weakening the immune response. Specifically for hair restoration surgery, patients should also be aware that cannabis may adversely impact hair growth depending on the levels of THC vs CBD in the products they are using (13).

7. Conclusion

The observation of increased local anesthetic requirements in some cannabis users is poorly understood and is likely influenced by multiple factors. Variability in cannabis dosing based on the product and mode of consumption along with individual responses to both cannabis and anesthetic agents complicates the ability to generalize findings, highlighting the need for further research to uncover the precise mechanisms involved. Hair restoration surgeons must be cognitive of factors such as frequency of cannabis use, dosage, the specific cannabinoids consumed, and the unknown individual pharmacogenomics which can impact metabolism as these may all contribute to altered anesthetic needs requiring adjustment in the operative plan during surgery.

Clinicians must adopt a patient-centered approach, tailoring anesthetic management to the unique characteristics and cannabis consumption habits of each individual. If patients are amenable to weaning off this drug preoperatively a few weeks prior to surgery, the risk of withdrawal symptoms can be mitigated. Effective management of the increasing numbers of patients who regularly use cannabis includes thorough preoperative assessment of cannabis use (type and frequency) with conservative planning for case size (graft numbers) to limit the expected duration of surgery, careful intraoperative monitoring and local anesthetic dose adjustment to avoid toxicity, and vigilant postoperative care to ensure effective pain control and management of possible withdrawal symptoms to facilitate recovery.

Ethics approval

Not applicable. The authors declare that human ethics approval was not required for this article.

Consent to participate

Not applicable.

Consent for publication

Not applicable.

Code availability

Not applicable.

Author's contributions

Conceptualization, AKG & SAK; Methodology, MT; Resources, AKG; Writing – Original Draft Preparation, MT, AKG & SAK; Writing – Review and Editing, AKG, MT & SAK.

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