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FEATURES OF ANESTHESIA IN PATIENTS WITH SPECIAL NEEDS. PART 3.

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To attain true knowledge, one must first feel doubt.
Aristotle, 4th century BC

Abstract. Over the past decade, the prevalence of cannabis use among patients requiring surgery has increased by more than 3.5 times, with currently one in seven surgical patients reporting cannabis consumption. Adjusted analysis demonstrated a 1.19 times increased risk of postoperative morbidity and mortality in cannabis users compared to non-users. Despite some discrepancies in the conclusions of many researchers regarding the impact of preoperative cannabis use on specific details of the postoperative period, all authors unanimously confirmed significant harm from cannabinoid dependence to patients' health. Pathological conditions caused by cannabis use are independent risk factors for postoperative complications, increased rates of rehospitalization and surgical interventions, prolonged hospital stays, and increased financial costs. Anesthesiologists' and surgeons' awareness of the pathophysiology of cannabis-dependent individuals will help prevent severe postoperative complications in this patient population and reduce the cost of surgical treatment. Medical cannabis-based preparations will undoubtedly be quite useful in the treatment of many diseases and pathological conditions, but they should be thoroughly studied prior to use in multicenter randomized controlled trials focusing on potential side effects in accordance with regional conditions.

Keywords: cannabis, postoperative period, analgesia, complications, withdrawal syndrome.

INTRODUCTION

There is currently growing interest in the influence of cannabis use on postoperative therapy [1, 2]. In the available medical literature, there are some discrepancies in the conclusions of many authors regarding the impact of preoperative cannabis use on specific details of the postoperative period. An analysis of information sources allowed us to study and systematize the pathophysiological features, postoperative complications, and their treatment in users of cannabis products.

EVIDENCE ACQUISITION

Articles for inclusion in the study were selected if they (1) were published in English, Ukrainian, or German, (2) reported health disorders associated with cannabis use, (3) reported on the interaction of cannabis with analgesic medications, (4) informed about the pathogenesis of cannabis withdrawal syndrome and its treatment, and (5) used an observational study design (cohort or cross-sectional). A retrospective information search was conducted from 2007 to 2024 using a spatial-vector model of the descriptor system, based on classifiers, supplemented by manual searches of the reference lists of included articles. 93.2% of the literature sources used were published in the last 5 years, 98.6% in the last 10 years, and 1.4% in earlier years.

EVIDENCE SYNTHESIS

Over the past decade, the prevalence of cannabis use among patients requiring surgical intervention

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has increased by more than 3.5 times ($p < 0.001$) [3], with currently one in seven surgical patients reporting cannabis consumption. In such patients, physicians should consider the increased risks associated with the need for enhanced postoperative medical care [4, 5]. The presence of narcotic dependence and potential risks of postoperative complications are often minimized by cannabis-dependent individuals (CDIs), who may consciously conceal their use of cannabis products [1].

Medical cannabis has gained clinical use in many countries for pain relief and the treatment of spasticity in multiple sclerosis, sleep disorders, chemotherapy-induced nausea and vomiting, anorexia, certain dermatological and viral diseases, and more [6, 7]. Although cannabis use in the postoperative period may potentially be beneficial, the research base on this issue in Ukraine is clearly insufficient. Cannabis use is associated with negative clinical consequences that can progressively worsen. These include an increased risk of cannabis use disorder, cognitive impairments, drug interactions due to polypharmacy, adverse reactions due to numerous diseases, injuries, surgical interventions, and intensive care [4, 8-10]. Currently, the results of informative clinical reports are somewhat conflicting: some studies demonstrate adverse outcomes in CDIs such as paranoia, anxiety, dry mouth, dizziness, abdominal pain, hyperemesis, substance dependence, cardiovascular and postoperative complications, hyper- or hypocoagulation, while others report positive effects (improved quality of life, pain reduction, and even reduced financial costs) [2, 10]. A corrected analysis of the National Inpatient Sample in the USA over the past 5 years for adult patients who underwent major elective inpatient surgeries demonstrated a 1.19 times increased risk of postoperative morbidity and mortality in CDIs ($p = 0.01$) compared to the non-dependent group [11]. Patients were classified based on their history of cannabis use: non-users, former users, or active users [12].

There is a growing interest in the impact of cannabis use on postoperative analgesic therapy [1, 2]. It is now known that cannabinoids are used in some countries as an adjunct in the treatment of chronic pain. Literature sources more often report the use of lower doses of opioids for pain relief in CDIs, but other reports claim the opposite [13]. Preclinical studies indicate that cannabinoids exert antinociceptive and antihyperalgesic effects, but their effectiveness in pain syndromes remains unclear. Using an experimental pain model in healthy volunteers, some researchers have shown that inhaled cannabis has a delayed biphasic effect on pain measures: a low dose had no effect, a moderate dose significantly reduced pain, and a high dose significantly increased it [14].

On the day of surgery, many identified cannabis users reported sleep disturbances, anxiety, and depression ($p < 0.01$) [5, 15, 16]. Postoperative pain scores were significantly higher in CDIs and in those who received high doses of nabiximols [8, 15, 17]. CDIs had a higher mean pain score at rest (62.3% vs. 45.5%; $p = 0.004$) and during movement (85.7% vs. 75.2%; $p = 0.021$) [12,17-20]. A significant amount of research shows that cannabis users more frequently report higher-than-real pain scores and require more analgesic medications in the immediate postoperative period following maxillofacial, orthopedic, abdominal, and oncogynecological surgeries compared to non-dependent patients [12, 16, 18-28]. CDIs required a 23 % higher postoperative morphine dose, approximately 12 morphine milligram equivalents (MME) [1, 2, 20]. Cannabis users had a 17.1 % higher mean pain score at 1 week compared to the control group ($p = 0.05$) [29,30]. They were prescribed more opioids during the first 14 days after surgery ($p = 0.23$) [31, 32]. There are several theories regarding the modulation of cannabinoid type CD1 and CD2 receptors in CDIs, which may lead to reduced receptor regulation, internalization, and desensitization after prolonged exposure. Opioid and cannabinoid receptors are localized in the spinal cord, periaqueductal gray, and rostral ventromedial medulla, which are involved in pain processing. The analgesic effects of cannabinoids are partially mediated by Δ- and κ-opioid receptors, which may explain the interaction between them. Another hypothesis is that cannabis users intentionally increase their doses before surgery because they believe that cannabinoid products may be effective for pain treatment (recent prospective population-based survey confirmed this). However, despite these expectations, the results of clinical trials investigating the analgesic efficacy of cannabinoids have been mostly disappointing, demonstrating only moderate evidence of chronic pain relief and no advantage over placebo for acute pain treatment [2, 12].

In the longer term after surgery, data on the need for narcotic analgesics are conflicting. Preoperative cannabis use was not independently associated with increased inpatient or outpatient opioid consumption during the 90 days following elective surgeries, and no correlation was observed between opioid doses and cannabinoid dependence [15, 33]. Other authors reported that 60 days after surgery, the need for opioids in cannabis-dependent individuals decreased below the levels of the control group ($p=0.018$) [34]. The average daily opioid consumption in MMEs during 0-6 months after surgery was 94.6 for non-users, 58.6 for former users, and 76 for active cannabis users ($p=0.139$). Within 6-12 months after surgery, these figures decreased to 39.9, 18.4, and 5.7, respectively

(p<0.0001) [12]. This discrepancy in results can be explained by the insufficient «purity of the study», due to the heterogeneous continuation of pill use in the postoperative period. A meta-analysis of preclinical studies showed that simultaneous administration of cannabis reduces the mean effective dose of morphine and codeine. According to the results of the European Quality of Life Questionnaire – 5D (EQ-5D) questionnaire, marijuana users, according to their own assessments, were younger, less healthy compared to non-users of cannabis, and had higher Medicaid insurance rates [10]. Marijuana users and non-users were compared regarding the use of analgesic drugs (including non-opioids), the frequency of chronic pain diagnoses, and pain tolerance by self-assessment. EQ-5D scores were 11.2 % lower in CDIs than in the control group. Both marijuana users and non-users were prescribed a certain amount of opioids during the first 14 days after surgery (176 ± 148 vs. 115 ± 87 MME). Multiple linear regression analysis showed that non-use of marijuana, as well as lower preoperative EQ-5D scores, were associated with increased opioid consumption during the first three postoperative days [31], as the comorbidities observed in CDIs are independent risk factors associated with increased complications in the postoperative period [4, 10].

Although patients using cannabis in the postoperative period ultimately receive more opioids or consume them for a longer period, they are much less likely to continue using them for more than 90 days after surgery. Preoperative cannabis use, as self-assessed, significantly reduced the number of patients who consistently used opioids, from 5 % to 1.4 % over this period. These findings help explain the role of cannabis as an adjunct treatment for acute postoperative pain and for preventing persistent opioid use in chronic postoperative pain [35]. Physicians should ensure careful collection of preoperative narcological history and properly inform patients about the associated risks [9].

During the postoperative period, individuals with cannabis use disorder (CUD) often experience psychiatric disorders such as psychosis, dysphoria, or euphoria, withdrawal symptoms, sedation, temporary decrease in muscle coordination, headache, blurred vision, ringing in the ears, and ataxia [24, 36]. Cannabis users are mostly young men who more frequently suffer from comorbid psychiatric disorders and schizoaffective disorders [4]. They have a stronger association with anxiety and depressive states (33.3% vs. 16.7%; p=0.01) [2,4]. Cannabis users experience poorer quality and higher frequency of sleep interruptions in the early postoperative period [1, 15, 18, 20, 21, 22, 24, 37]. Illegal recreational cannabis use in the postoperative period often leads to conflict situations and numerous adverse incidents of early (unplanned) discharge due to violation of hospital rules ($p < 0.001$) [9, 12].

Postoperative ischemic stroke remains the most common vascular side effect in individuals with cannabis use disorder (CUD). Most cells involved in controlling cerebrovascular regulation can produce endocannabinoid ligands (anandamide and 2-arachidonoylglycerol) and express CB-R receptors, leading to the synthesis of endothelial vasodilators that can increase cerebral blood flow (CBF). However, under certain metabolic stress situations (hypoxia, hypercapnia), CB-R activation actually decreases CBF by inhibiting neuronal metabolism and synaptic electrical activity. Recent studies have shown that the frequency of cerebrovascular ischemia in young (25–35 years old) marijuana users is 2.3-2.9 times higher ($p = 0.007$) than in non-users [9, 12, 21]. A recent review of observations in cannabis users identified an increase in cerebrovascular ischemic events [32]. Adjusted odds for acute cerebrovascular events were 1.6 to 3.3 times higher for CUD ($p < 0.019$) [3,38].

Peak plasma concentration of Δ9-tetra-hydrocannabinol (THC) is associated with an increase in systolic blood pressure by 20–100 % compared to baseline values. Some reports, including echocardiographic assessments of cardiac function, have shown increased cardiac output and premature ventricular contractions. Initial tachycardia may be mediated by the β-adrenergic effect of adrenaline (stimulation of the adrenal glands) along with suppression of the parasympathetic nervous system. Pretreatment with propranolol effectively blocked THC-mediated increases in heart rate. Similarly, tachycardia, impairment of left ventricular contractility, and cardiac output have been reported in experienced users after daily marijuana consumption (THC ≥ 10 mg). Chronotropic and inotropic effects are enhanced by synthetic cannabinoids and suppressed by the administration of CB1-R antagonists (rimonabant). At usual high doses of cannabinoids, a strong parasympathetic reaction manifests as arterial hypotension and bradycardia in the patient's horizontal position. Prolonged sympathetic stimulation may be insufficient to compensate for these postural hemodynamic changes, resulting in orthostatic hypotension due to peripheral vasodilation and baroreflex dysregulation. Interestingly, after controlled administration of high doses of THC in chronic users, a decrease in heart rate and tolerance to orthostatic hypotension was reported [21].

Among patients with substance use disorders, a higher frequency of arrhythmias is observed compared to non-drug-dependent individuals (2.7 % vs. 1.6 %) [5, 39]. The prevalence of cannabis-related arrhythmias has doubled over the past decade. Men

aged 45 to 64 belong to the higher-risk group, with atrial fibrillation being the most common arrhythmia. Atrial flutter, second-degree atrioventricular block, ventricular tachycardia, ventricular fibrillation, Brugada syndrome, and asystole are also serious rhythm disorders associated with marijuana use. Acute cardiovascular effects include tachycardia and vasodilation, which may increase the frequency of coronary ischemia in the at-risk group [39, 40]. Acute myocardial infarction has mostly been associated with the previous use of synthetic cannabinoids [21, 41, 42]. The adjusted odds ratio for postoperative myocardial infarction in patients with substance use disorders is 1.88 times higher ($p < 0.001$) compared to non-substance-dependent patients [3, 24, 38, 39].

Cannabis use is associated with premature aging of the cardiovascular system, arterial stiffness, and microvascular integrity changes [42]. Inflammatory response of the arterial wall and increased oxidative stress, platelet activation, and excessive activation of factor VII have been proposed as the main mechanisms of THC-induced platelet aggregation. Additionally, cannabinoids may reduce the availability of nitric oxide in blood vessels, leading to endothelial dysfunction and platelet activation [21]. During the postoperative period, cannabis users and substance-dependent patients had similar in-hospital mortality rates, but perioperative pulmonary embolism rates were 2.2 times higher ($p = 0.005$) [9, 12, 21]. They also had 1.7 times higher rates of deep vein thrombosis [43] and higher risks of postoperative major bleeding, with advanced age being an independent risk factor for such complications [7]. Acute kidney injury, mostly of vascular origin, in the postoperative period in patients with substance use disorders occurs 1.51 times more frequently than in non-drug-dependent individuals ($p = 0.05$) [41].

A recent analysis of postoperative care for substance uses disorder patients showed an increase in the incidence of hypothermia [32]. However, the frequency of postoperative tremor, which can lead to hypoglycemia, was 40 % among cannabis users compared to 33 % among non-users [21].

Regular THC consumption negatively affects respiratory rate, tidal volume, CO_2 retention, and is a risk factor for developing pneumonia or bronchitis [42]. In patients with substance use disorders, several clinical studies have reported a higher frequency of postoperative respiratory complications ($p < 0.001$) [7, 9, 12, 41], an increase in cases of airway hyperreactivity [32], decreased lung function, and complaints of upper respiratory tract symptoms [36]. Preoperative cannabis smoking is associated with postoperative airway obstruction characterized by swelling of the throat and tongue. Diffuse alveolar hemorrhage and necrotizing bronchiolitis have been associated with high-dose THC inhalation, accompanied by inflammatory swelling and increased permeability of capillary walls, which may be exacerbated by the antithrombotic effect of cannabinoids [21]. However, some researchers do not note a clinically significant association between cannabis use and hypoxia or combined pulmonary complications [16, 44, 45].

Marijuana use is associated with dysfunction of the hypothalamic-pituitary-gonadal axis. Chronic cannabis use acutely lowers testosterone levels until tolerance develops, after which levels normalize. Chronic cannabis use leads to decreased growth hormone production, sperm count reduction, and the development of gynecomastia in men. Several studies in women have demonstrated changes in menstrual cycle hormones and an increased risk of infertility. Marijuana use during breastfeeding may suppress lactation through its effects on prolactin [40].

CB2 receptors are located in the immune system and nerve endings and are responsible for certain reactions, including the modification of pro-inflammatory substance expression by macrophages, neutrophils, and subsets of B and T cell immunity [46]. In particular, dental patients diagnosed with cannabis use had an increased risk of site infection, facial nonunion, facial abscess, etc. [47]. In the substance use disorder group, there were 8.6 % active fistulizing diseases or intra-abdominal abscesses compared to 5.9% ($p < 0.001$) in non-drug-dependent individuals [46], and septic conditions occurred 2.39 to 3.55 times more frequently ($p = 0.031$) than in the control group [7, 9, 12, 41]. However, there are reports of certain bactericidal and fungicidal properties of hemp terpenes, which require further investigation [48].

Stimulation of CB1 receptors in the liver may contribute to the development of steatosis by enhancing lipogenesis, reducing fatty acid oxidation, and inducing hyperphagia [46]. Preoperative marijuana use has been associated with increased postoperative use, which may hinder weight loss and increase the risk of weight regain [49]. Gastric emptying is delayed, leading to early satiety, which may serve as a weight loss strategy, despite well-known central nervous system appetite stimulation and modification of nausea [46]. Studies in bariatric surgery have not shown an increased risk of short-term surgical complications or differences in weight loss over 2 years post-surgery among marijuana users [50, 51].

Chronic cannabis use may lead to nausea, vomiting, and abdominal pain and may be a risk factor for the development of Barrett's esophagus at a younger age and in populations where Barrett's disease is not typically prevalent [52, 53]. Activation of CB1 receptors reduces motility along the gastrointestinal tract mainly by inhibiting the release of contractile transmitters. Cannabinoids can cause a wide range of physiological

reactions, such as gastrointestinal motility, intestinal secretion, inhibition of inflammatory mediators, promotion of fibrosis, as well as control over CNS mood, pain, and appetite [46]. Abdominal visceral pain in irritable bowel syndrome is explained by increased perception of colon distension in approximately 70 % of patients, and this visceral sensation is partially mediated through cannabinoid receptors. Cannabinoid dependence is associated with an increased risk of pancreatitis. Liver CB1 receptors may also stimulate fibrogenesis, especially in alcoholic hepatitis [46].

Cannabinoid hyperemesis syndrome is an adverse effect of long-term (≈ 6–7 years) daily and weekly cannabis use, characterized by periodic episodes of severe nausea, vomiting, abdominal pain, and diarrhea [25, 53-55], formerly known as cyclic vomiting syndrome. It occurs exclusively in patients who smoke cannabis regularly (daily for many years), rather than in individuals who only use marijuana orally. Low doses of cannabidiol (CBD) have antiemetic properties, while higher doses cause a proemetic effect. Some authors describe a lower frequency of postoperative vomiting in cannabis-dependent patients compared to non-users (9.6 % vs. 12.6 %), which may be explained by continued cannabis use in small doses in the early postoperative period [5].

In the clinical course of cannabinoid hyperemesis syndrome (CHS), three phases are distinguished:

– prodromal phase: morning nausea, fear of vomiting, and nonspecific abdominal discomfort, which can last from months to years;
– hyperemetic phase: development of severe nausea, intractable vomiting, and diffuse abdominal pain, prompting medical evaluation;
– recovery phase: characterized by improvement of symptoms from weeks to months after cessation of cannabis use, with gradual weight restoration resulting from a return to normal mood and eating patterns [46, 56].

Diagnostic characteristics of cannabinoid hyperemesis syndrome (CHS) include a history of regular cannabis use at any time (100 %), cyclic nausea and vomiting (100 %), symptom relief after cessation of cannabis use (96.8 %), compulsive hot baths with symptom relief (92.3 %), predominance in males (72.9 %), abdominal pain (85.1 %), and at least weekly cannabis use (97.4 %) [57, 58]. Patients with substance use disorders may be at increased risk of postoperative nausea and vomiting after general anesthesia [37, 54, 59-63]. CHS is often resistant to standard antiemetic medications [64]. A recent retrospective cohort study showed an association between chronic cannabinoid use and approximately a 20 % increase in the frequency of postoperative nausea and vomiting [7, 20], with higher frequencies among daily (21.9 %) and current users (18.8 %) compared to non-users (17.3 %) [37].

The chronic effects of THC lead to its accumulation in fat cells. Its prolonged supranormal level desensitizes and reduces the regulation of CB1 receptors, thereby enhancing the stress response, which, in turn, can induce CHS. CBD is an antiemetic at low doses but induces vomiting at high doses. Like THC, the accumulation of cannabidiol in chronic cannabis users may also be a triggering factor for CHS. Patients with CHS may have genetic variations in liver enzymes involved in drug metabolism, leading to excessive levels of cannabis metabolites and promoting vomiting [56, 64].

Although cannabis and synthetic cannabinoids are used to treat postoperative nausea and vomiting, their effectiveness for treating CHS is not established. Withdrawal symptoms after discontinuation of chronic cannabis use include nausea, irritability, restlessness, sleep disturbances, anxiety, depressed mood, and physical discomfort. Abdominal pain typically begins within 24–48 hours, depending on the type of cannabinoid used, route of administration, frequency, and dose. Withdrawal symptoms from cannabinoids are more severe in women, although nausea is less common in them than other withdrawal symptoms. While withdrawal symptoms typically emerge within a few days, the impact of emetogenic stimuli (such as anesthetics and analgesics, peritoneal stretching) in combination with reduced or discontinued cannabis use in the postoperative period may precipitate withdrawal symptoms earlier than expected [37].

Evidence of high quality for pharmacological treatment of CHS is extremely limited. Both oral nabilone and intravenous THC are unable to provide adequate prophylaxis, and currently, no form of cannabis is used to treat this form of nausea and vomiting [18, 19]. Benzodiazepines are most considered effective for treating acute CHS, followed by haloperidol (more effective than ondansetron) and topical capsaicin cream. As the prevalence of CHS is likely to increase, future prospective trials are essential to assess and further define the optimal pharmacological treatment of patients with CHS [46, 56, 58, 64]. Hot showers and baths have been universally effective in mitigating or reducing the manifestations of CHS. Several theories have been proposed to explain this mechanism. One theory is the dose-dependent hypothermic effect of THC on CB1 receptors in the hypothalamus, the brain's thermoregulatory center. «Skin stripping» syndrome is another anticipated mechanism, in which skin vasodilation from hot water alters internal temperature and splanchnic circulation, thus reducing abdominal discomfort. Another possibility is that the dysphoria and anxiety associated with CHS may be subjectively alleviated by a hot shower or bath [58, 64].

In the postoperative period, two main aspects should be considered for patients using marijuana: problems with postoperative pain management and alleviation of withdrawal symptoms [21]. Increased pain despite higher opioid consumption and sleep disturbances indicates withdrawal symptoms and possibly hyperalgesia [1]. Regular cannabis consumption is associated with desensitization and downregulation of human cortical and subcortical CB1 receptors. This begins to change within the first 2 days of abstinence, and receptors return to normal functioning within ~4 weeks, which may represent neurobiological time frames for the duration of Cannabis Withdrawal Syndrome (CWS), not accounting for cellular and synaptic long-term neuroplasticity [65]. Postoperative cessation of cannabis use may result in signs and symptoms of CWS, including hypertension and tachycardia [3]. The Eleventh Revision of the International Classification of Diseases (ICD-11) includes cannabis-induced psychotic disorder, characterized by «psychotic symptoms developing during or soon after cannabis intoxication or withdrawal» [66]. Cannabis withdrawal refers to symptoms that occur after abrupt cessation or significant reduction in THC consumption. Discontinuation of short-term CBD use, a non-psychoactive cannabinoid, does not result in withdrawal syndrome [67, 68]. Synthetic cannabinoids can be 2–100 times more potent than THC, leading to more severe withdrawal than natural cannabis [26, 68]. Withdrawal symptoms typically begin within 24–48 hours after cessation of use. The early withdrawal phase is typically characterized by sleep disturbances/nightmares, irritability, anxiety, decreased appetite, tremors, and, less commonly, sweating, chills, headache, physical tension, and abdominal pain. These early symptoms typically peak within 2-6 days. They improve as THC levels decrease over the first 7 days of abstinence. Anger, aggression, and depressive mood may occur as early as 1 week after cannabis cessation, but they usually peak within 2 weeks of abstinence. Sleep disturbances may persist for several weeks or longer. Cannabis withdrawal syndrome is more common among men, but women may experience more severe CWS symptoms than men [67-69]. Patients with Type A CWS experience peak symptom intensity between 2 and 6 days after last contact. Patients showing progressive symptom intensity reduction after cannabis cessation are classified as Type B CWS [21]. Withdrawal onset can occur within 1–2 days after the last cannabis use and last 1–2 weeks; thus, healthcare providers should monitor signs of cannabis withdrawal in postoperative patients until cannabis use is resumed [21, 22].

Currently, there are no medications approved for the treatment of cannabis withdrawal syndrome [68]. Diazepam is used to treat anxiety, agitation, and sleep disturbances. Improvement of CWS is caused by dronabinol, nabiximols, and gabapentin. Zolpidem and extended-release mirtazapine improve certain sleep features, while nabilone reduces cravings and anxiety. However, divalproex does not reduce irritability, depression, and anxiety, and topiramate does not improve mood. Nausea and stomach pain are treated with metoclopramide, hyoscyamine, and promethazine. Antipsychotics (olanzapine, quetiapine) are prescribed for psychotic symptoms/hallucinations, while other antidepressants, atomoxetine, lithium preparations, and buspirone have not shown a relevant effect [62, 65, 68, 70, 71]. The «black box» warning about prolonged QT interval syndrome associated with butyrophenone neuroleptics should not preclude their use in CWS, but ECG monitoring is desirable before administration [62]. When prescribing dexmedetomidine at a dose > 1.0 mcg/kg/hr, there is a significant risk of arterial hypotension and bradycardia [72].

A hypothesis was put forward that patients using marijuana are more likely to require a higher level of medical care after surgical intervention, including unplanned intensive care unit admission, readmission, or discharge from the healthcare facility after emergency care [4].

Since cannabis users have a 2.24 times higher frequency of postoperative complications than non-users ($p < 0.003$), this is associated with a significant increase in the overall cost of medical services and length of hospital stay [7, 41, 70]. Doses of cannabis consumed directly correlate with a higher risk of complications and increased hospitalization duration by 1.3 to 1.6 times ($p < 0.001$), but not with in-hospital mortality compared to non-users [7, 9, 41, 43]. Some authors did not find a statistically significant difference in bed-days between the cannabis group and non-users [3, 9, 12], as compared to the control group, pill users were 1.45 times more likely ($p = 0.0007$) to have non-routine (forced) discharge home and had a 30 % lower chance of rehabilitation ($p = 0.0013$) [10].

The total cost of medical services was higher in the cannabis group on the day of surgery ($14,024.88 vs. $12,127.49; $p < 0.0001$), while simultaneously incurring significantly higher daily ($22,614 vs. $17,955; $p < 0.0001$), overall ($58,507 vs. $50,924; $p < 0.0001$), and 90-day material costs ($19,155.45 vs. $16,315.00; $p < 0.0001$) compared to non-cannabis-dependent patients [10, 41, 43].

The emergency department visit rate within six months post-operation was 13.2 % for non-marijuana users, 18.2 % for previous marijuana users, and 15.4 % for active marijuana users ($p = 0.0001$) [12, 28, 41, 43]. The frequency of readmissions within 30 days was 1.36 times higher [4], and within 90 days, it was

significantly higher at 11.6 % compared to 6.0 % (p = 0.042) [7]. The frequency of readmissions within one-year post-operation was 12.6 % for non-marijuana users, 9.1 % for previous marijuana users, and 15.4 % for active users (p = 0.0001) [12, 41, 43].

Patients with cannabis use disorder have decreased bone mineral density and an increased risk of fractures [7]. The level of non-union fractures in this group was higher (2.4 %) compared to the control group (1.1 %) [39]. Active preoperative cannabis use may be associated with a 1.69 times higher frequency of reoperations after surgical treatment of mandibular fractures compared to non-users [47]. The rate of reoperations (including major amputations) within two years was 4.0 % for non-marijuana users, 0 % for former cannabis users, and 23.1 % for active users (p = 0.0075) [12, 41]. Marijuana use (p = 0.041) significantly increases the likelihood of a repeat spine surgery within 3 years after primary lumbar spinal fusion [73].

Since preoperative cannabis use may be a risk factor for increased rates of reoperations and postoperative opioid requirements, anesthesiologists and surgeons should be well informed about their patients' history of cannabis use, as well as the overall impact of cannabis on post-anesthesia and postoperative outcomes [12, 74].

CONCLUSIONS:

1. Despite certain discrepancies in the findings of many researchers regarding the impact of preoperative cannabis use on specific details of the postoperative period, all authors unanimously confirmed the significant harm of cannabinoid dependence to patients' health.
2. Pathological conditions caused by cannabis use are independent risk factors for postoperative complications, increased rates of readmissions and surgical interventions, length of hospital stay, and material costs.
3. Awareness of anesthesiologists and surgeons about the pathophysiology of cannabis-dependent individuals will help prevent severe postoperative complications in this patient population and reduce the cost of surgical treatment.
4. Medical cannabis-based products will undoubtedly be quite useful in treating many diseases and pathological conditions, but they must be thoroughly studied based on the principles of multicenter randomized controlled trials focusing on potential side effects in accordance with regional conditions.

As the progressive spread of creative cannabinoid use among the population and the legalization of medical cannabis are likely to affect the initial health status of surgical patients, the authors hope that the provided information will be useful for anesthesiologists, surgeons, and professionals in other medical specialties in their everyday practice.

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ОСОБЛИВОСТІ АНЕСТЕЗІЇ В ПАЦІЄНТІВ ЗІ СВОЄРІДНИМИ ПОТРЕБАМИ. ЧАСТИНА 3

Абстракт. За останнє десятиліття поширеність вживання канабісу серед пацієнтів, які потребують хірургічного втручання, зросла більш ніж у 3,5 рази, і наразі кожен сьомий пацієнт, якому було виконано оперативне втручання, повідомляє про вживання канабісу. Скоригований аналіз продемонстрував підвищення у 1,19 рази ризику післяопераційної захворюваності та смертності у вживачів марихуани, порівняно з тими, хто не вживає канабіс. Не зважаючи на деякі розбіжності у висновках багатьох дослідників щодо впливу передопераційного вживання канабісу на окремі деталі післяопераційного періоду, усі автори одностайно підтвердили значну шкоду канабіноїдної залежності для здоров'я пацієнтів. Патологічні стани, спричинені вживанням канабісу, є незалежними факторами ризику післяопераційних ускладнень, збільшення частоти повторних госпіталізацій та хірургічних втручань, тривалого перебування в лікарні та збільшення фінансових витрат. Обізнаність анестезіологів і хірургів щодо патофізіології залежних від канабісу осіб допоможе запобігти важким післяопераційним ускладненням у цієї категорії пацієнтів і знизити вартість хірургічного лікування. Препарати на основі медичної коноплі, безсумнівно, будуть досить корисними при лікуванні багатьох захворювань і патологічних станів, але їх необхідно ретельно вивчити перед клінічним використанням у багатоцентрових рандомізованих контрольованих дослідженнях з акцентом на можливі побічні ефекти відповідно до регіональних умов.

Ключові слова: канабіс, післяопераційний період, знеболювання, ускладнення, абстинентний синдром.

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