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Case Report

Case Report: Formulation of Balanced Medicinal Cannabis in the Tapering of Opioids in Non- Cancer Chronic Pain

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ABSTRACT

This case report discusses the management of chronic non-oncologic pain in a 28-year-old female patient with spinal cord injury using a balanced medicinal cannabis formulation. The patient, initially on opioids and gabapentin, underwent multiple pharmacological interventions, including Tapentadol and Pregabalin, with variable success. Eventually, a balanced cannabis formulation (THC 12 mg/ml - CBD 14 mg/ml) allowed for successful opioid tapering, resulting in improved pain control and reduced anxiety symptoms. Psychiatric and toxicology evaluations were recommended but not attended. This case highlights the potential of medicinal cannabis as an alternative therapeutic option in opioid management for chronic pain.

Keywords: Chronic pain management; Medicinal cannabis; Opioid use disorder; Clinical case report; Clinical management; Quality of life; Spinal cord injury; Cannabinoids; Palliative care; Integrative medicine

Introduction

The World Health Organization (WHO) defines a drug as any substance that, when introduced into the body by any route of administration, can alter the central nervous system in some way. Therefore, the term drug dependence is understood as the habit of consuming drugs, accompanied by phenomena of tolerance and dependence, with drug-seeking behaviors taking precedence over other important priorities despite knowing that it can cause mental or physical harm to the individual[1].

Disorders associated with drug use constitute a significant public health problem. In the Americas, 85,984 deaths attributable to the consumption of illicit psychoactive substances

were reported in 2019, representing a 296% increase since 2000[2]. Regarding the abuse of licit drugs, opioids, which are considered widely used molecules for managing chronic pain, have been associated with a high risk of misuse, abuse, diversion, addiction and overdose deaths[3]. Opioid-related deaths have increased by approximately 20% since 2011, with significant increases in the United States, followed by Canada[4]. In response to this issue, comprehensive public policies have been promoted, aimed at increasing controls on sales, advertising, availability and the strict prescription of this class of medication through evidence-based clinical guidelines[4].

Assessing pain as a biopsychosocial experience involves a rigorous individualized analysis of the risk/benefit ratio of initiating opioid-based therapy[5]. Risk factors associated with opioid use disorders (OUD) include young age (18 to 25 years), male gender, psychiatric disorders, exposure to violence or sexual assault, history of substance use and family history of substance use disorders[6]. Therefore, it is important to assess the risk of potential opioid misuse before initiating treatment[7]. To date, specific treatments for prescription opioid use disorders are limited and usually involve supervised detoxification, followed by a maintenance phase with longer-acting opioid substitution therapies with less euphoric effects over extended periods. Methadone and buprenorphine are the most common substitution therapies, with highly variable efficacy rates[8].

Medicinal cannabis has been associated with an analgesic effect, leading to its increased use in 34 combinations with opioids[9]. A systematic review in 2020 evidenced a reduction of 64% to 75% in opioid doses when used in combination with medicinal cannabis in patients with non-cancer chronic pain[10]. However, the emergence of high-risk biases in the studies analyzed in this review prevents establishing a clear causal relationship. Consequently, there remains a need to generate scientific evidence to clarify whether the combination of opioids and cannabis in the treatment of non-cancer chronic pain truly influences the reduction of opioid doses. Hence, the purpose of this article is to present the case of a patient with non-cancer chronic pain who was treated with a balanced cannabis formulation, which allowed her to gradually discontinue opioids. This case suggests that the use of balanced cannabis could be considered a viable therapeutic option in pain management.

Methods

Patient consent and data usage

Written informed consent was obtained from the patient for the publication of this case report and the use of her clinical data (Annex 1).

Ethical considerations

This study was conducted in accordance with the principles outlined in the Declaration of Helsinki.

Clinical management

The patient's clinical management included a multidisciplinary approach involving pharmacological interventions such as gabapentin, opioids and eventually a balanced chemotype II medicinal cannabis formulation. Treatment decisions were guided by clinical evaluations and adjustments made based on patient response and symptom management needs.

Case Report

The patient, a 28-year-old woman from Bogotá, single and employed as a security guard, presented to the medical clinic with a two-month history of symptoms. She had sustained a gunshot wound resulting in a spinal cord injury (SCI) classified as ASIA A, with a complete spinal cord transection at the T11 sensory level. Additionally, multiple fractures of the spinous processes and laminae of the L2 vertebra were observed.

Due to the severity of her injuries, the patient underwent emergency surgery at Hospital Meissen in Bogotá for trauma damage control. The surgical procedures included a left nephrectomy, drainage of a 100 ml hemothorax via left thoracotomy, left phrenorraphy, resection of the splenic flexure of the colon and the creation of a double-barrel colostomy. Multiple peritoneal lavages were performed and dynamic abdominal wall closure using a VAC system was implemented.

The patient experienced somatic and neuropathic pain in her lower limbs, which was difficult to control with the prescribed analgesic regimen, consisting of gabapentin 600 mg/day, acetaminophen 325 mg and hydrocodone 5 mg every 8 hours. Consequently, she was referred to the pain clinic. During the systems review, the patient reported poor sleep quality, chronic fatigue and symptoms of anxiety and depression. Her medical history included a diagnosis of depression, although she was not receiving active treatment at the time.

Regarding her pharmacological history, the patient was taking gabapentin 300 mg every 12 hours and acetaminophen plus hydrocodone 325/5 mg every 8 hours, but she did not experience significant pain relief. Additionally, she had a history of frequent recreational cannabis and alcohol use. Surgically, the patient had previously undergone an exploratory laparotomy that included a left nephrectomy, 100 ml hemothorax drainage via left thoracotomy, left phrenorraphy, resection of the splenic flexure of the colon, double-barrel colostomy, dynamic abdominal wall closure with VAC and multiple peritoneal lavages. Her gynecological and obstetric history was G1A1 and her family history revealed hypertension and heart disease in her parents and grandparents.

During the physical examination, the patient was in a wheelchair and had normal vital signs. She appeared anxious and was prone to crying easily. Neurologically, she was conscious, alert and oriented to time, place and person. There were no motor or sensory abnormalities in her upper limbs. However, in her lower limbs, she exhibited foot retraction, loss of deep tendon reflexes and absence of sensory and motor function, indicative of a complete T11 spinal cord injury. The patient used a knee-ankle-foot orthosis on her left lower limb, with thigh straps and a linear knee-ankle-foot joint with a ring lock in extension. Additionally, she had an indwelling urinary catheter and a functional colostomy.

The patient is diagnosed with mixed chronic pain secondary to deafferentation, uncontrolled, along with anxiety and depression and impulse control disorder. Therefore, it was decided to refer her to a comprehensive rehabilitation center for high-frequency physical rehabilitation therapy.

An adjustment was made to her analgesic regimen, administering gabapentin 400 mg every 8 hours and rotating to an atypical opioid (due to its mechanisms of action), acetaminophen plus tramadol 37.5 mg every 6 hours. In a subsequent rehabilitation medical board meeting, acetaminophen plus tramadol was discontinued and immediate-release tapentadol 50

mg every 8 hours was initiated for one month. Additionally, a multidisciplinary evaluation by Physiatry and Neurosurgery was requested.

One month later, the patient reported poor pain improvement with tapentadol and mentioned that a home physician had prescribed methadone 10 mg every 6 hours. During the evaluation, active affective symptoms and problematic methadone use were identified, with the patient being highly demanding during consultations and insisting on the need to use this opioid as the only relief for her pain. Occasionally, she became aggressive when unable to obtain the medication. Therefore, tapentadol was discontinued due to the unsatisfactory response and treatment was continued with gabapentin and methadone 10 mg every 6 hours. She was subsequently referred for toxicology and psychiatry evaluations due to affective and sleep disturbances associated with her clinical condition.

At the third month of follow-up, the patient attended a psychiatry evaluation and started treatment with duloxetine, titrated up to 120 mg/day, in combination with mirtazapine 30 mg/night. She did not attend the toxicology evaluation. During the fourth and fifth months of follow-up, it was proposed to restart tapentadol at a maximum dose of 500 mg/day, with 400 mg of extended-release and 100 mg of immediate-release using the following regimen: 200 mg in the morning, 200 mg in the evening and 50 mg as needed for breakthrough pain. Additionally, gabapentinoid neuromodulator was switched to pregabalin 300 mg every 12 hours. It was documented that the patient continued to receive methadone through home medical prescriptions, which she reported provided maximum improvement.

In subsequent follow-up visits up to one year, worsening opioid use disorder associated with methadone was evident, with methadone being the only medication that effectively controlled her pain and anxiety. The patient was evaluated by general medicine at her HMO, which discontinued methadone and started hydromorphone 5 mg every 6 hours, resulting in poor pain modulation.

Subsequently, methadone and pregabalin were continued by home medical care, with the patient increasingly demanding methadone refills. No continued psychiatric follow-up was documented and she did not attend the toxicology evaluation. It was decided to start treatment with balanced chemotype II cannabis (THC 12 mg/ml – CBD 14 mg/ml) with slow titration guided every 5 days starting from 0.1 ml.

During successive follow-up visits, a gradual reduction in the methadone dosage was observed. This process began with a 25% reduction in the daily dose during the first month, followed by another 25% reduction, reaching the 18-month follow-up mark, at which point the patient was taking half a tablet every 6 hours, approximately 10 days a month. By the end of this period, the dose was reduced to 5mg every 12 hours, resulting in a 40-50% reduction in pain with the treatment **(Table 1)**. At the 21-month follow-up, the patient reported that using the balanced chemotype II cannabis formulation at a dose of 0.2 ml in the morning and 0.3 ml in the afternoon eliminated the need for methadone and resulted in a 100% improvement in pain. However, there was a slight increase in cramps and occasional electric shock sensations, as reported by the patient, leading to an adjustment of pregabalin to 450 mg in the morning and 300 mg in the afternoon.

After 2 years of follow-up, it was possible to reduce the neuromodulator to a pregabalin dose of 300mg every 12 hours, completely discontinue the use of methadone and adjust the balanced cannabis formulation dose to 0.3 ml every 12 hours.

Table 1: Titration Regimen for Tapering Opioids in Non-Cancer Chronic Pain with Medicinal Cannabis.

Medical consultation number	Treatment	Management and Outcome
1	Gabapentin 300 mg every 12 hours, ACTM (Acetaminophen + Hydrocodone) 325 + 5 mg every 8 hours	Gabapentin 400 mg every 12 hours, rotated to ACTM + Tramadol 325 + 37,5 mg every 8 hours
2	Gabapentin 400 mg every 12 hours, rotated to Tapentadol 50 mg immediate release every 8 hours	Poor pain control. Psychiatry assessment of pain suggested.
3	Gabapentin 400 mg every 12 hours, metadone 10 mg every 6 hours was initiated	Started by home care doctor without considering analgesia in opioid rotation
4	Duloxetine 120 mg per day, mirtazapine 30 mg at night, followed by a toxicology assessment	Evidence of opioid use disorder (OUD)
5	Reinitiated Tapentadol 500 mg per day and rotated to Pregabalin 600 mg per day	Continues to receive methadone from home healthcare
6-7-8-9	Evidence of opioid use disorder (OUD) Metadone 10 mg every 6 hours, patient demanding formulation	A healthcare service provider prescribes hydromorphone instead of methadone.
10	The patient did not attend the follow-up appointments with toxicology or psychiatry.	Management begins with medicinal cannabis chemotype II THC12mg-CBD14mg/mL balanced, slow titration.
11	Methadone decreased by 25% this month.	The titration continues, reaching a dose of 0.2 mL in the mornings and 0.2 mL in the afternoons of medicinal cannabis and pregabalin continues at 300 mg every 12 hours.
12	Methadone decreased by 25% this month.	The titration continues, reaching a dose of 0.2 mL in the mornings and 0.2 mL in the afternoons of medicinal cannabis and pregabalin continues at 300 mg every 12 hours.
13	Methadone decreased by 25% this month.	The titration continues, reaching a dose of 0.2 mL in the mornings and 0.2 mL in the afternoons of medicinal cannabis and pregabalin continues at 300 mg every 12 hours.
14	Methadone decreased by 25% this month.	The titration continues, reaching a dose of 0.2 mL in the mornings and 0.2 mL in the afternoons of medicinal cannabis and pregabalin continues at 300 mg every 12 hours.

15-16-17-18	Rescue doses of 5mg/day of methadone and 750mg/day of pregabalin.	The titration continues, reaching a dose of 0.2 mL in the mornings and 0.2 mL in
		the afternoons of medicinal cannabis. Pregabalin continues at 450 mg in the mornings and 300 mg in the evenings.
19-20-21	Rescue doses of 5mg of methadone every 72 hours and 750mg/day of pregabalin	The titration continues, reaching a dose of 0.2 mL in the mornings and 0.3 mL in the afternoons of medicinal cannabis. Pregabalin continues at 450 mg in the mornings and 300 mg in the evenings.
22-23-24	Without rescue doses of methadone, pregabalin dose adjusted to 300 mg every 12 hours.	The titration continues, reaching a dose of 0.3 mL in the mornings and 0.3 mL in the afternoons of medicinal cannabis and pregabalin continues at 300 mg every 12 hours.
From 25 onwards	Pregabalin at 300 mg every 12 hours and medicinal cannabis chemotype II THC/CBD 12/14 mg/mL, 0.3 mL every 12 hours.	Pregabalin 300 mg every 12 hours and medicinal cannabis chemotype II THC/CBD 12/14 mg/mL, 0.3 mL every 12 hours.

Discussion

Opioids are widely used molecules for pain management; however, they have been associated with a high risk of abuse and dependence, leading to significant biological and emotional disorders that can profoundly impact health and quality of life[11]. Therefore, the prescription of these medications should be approached with scientific rigor, considering their pharmacokinetics, pharmacodynamics and individual risk factors, including toxic-allergic histories such as prior use of hallucinogenic substances or alcohol, which increase the risk of dependence, tolerance or addiction.

In this context, it is important to highlight the crucial role of the endocannabinoid system, which is composed of CB1 and CB2 receptors. CB1 receptors, primarily located in the brain, are not only associated with the psychoactive effects of cannabis but also with the regulation of stress, inflammatory response, emotions, appetite control and energy balance. On the other hand, CB2 receptors are predominantly found in the immune system, although they have also been identified in other cell types[12,13]. This system plays a critical role in modulating various physiological and pathological processes, underscoring its importance in understanding and managing conditions such as non-cancer chronic pain.

The most studied active principles in modulating the endocannabinoid system are cannabidiol (CBD) and delta-9-tetrahydrocannabinol (THC) derived from Cannabis spp. Subsequent research identified anandamide (AEA) as the first isolated endogenous compound, followed by 2-arachidonoylglycerol (2AG). Modulating this system has been considered to have great therapeutic potential in a wide range of diseases, including obesity, metabolic syndrome, diabetes, inflammatory neurodegenerative diseases, cardiovascular, hepatic and gastrointestinal diseases, as well as in pain management, psychiatric disorders, cachexia, anorexia and chemotherapy-induced nausea and vomiting[12-13].

Cannabis sativa is a plant with over 500 chemical compounds, including nearly 120 phytocannabinoids and 100 types of terpenes, the latter being volatile molecules that possess important pharmacological effects such as antidepressant, anxiolytic, bactericidal, fungicidal and sleep-inducing actions. Various studies have demonstrated a synergy between the compounds and together they exert a better therapeutic effect known as the entourage or ensemble effect, which also demands lower dosages compared to synthetic analogs.

Scientific literature on the use of medicinal cannabis in the treatment of opioid use disorder is limited, but it is considered a novel and promising alternative that should be evaluated only by healthcare professionals properly trained in its use. It is important to carefully monitor acute withdrawal symptoms[14].

A study by the National Academy of Sciences, Engineering and Medicine acknowledged that there is solid scientific evidence for the therapeutic use of medicinal cannabis in treating chronic pain in adults[15]. Chronic pain is one of the main drivers of the opioid epidemic in the United States. A JAMA report in 2014 recorded a 25% decrease in opioid-related deaths in states where medicinal cannabis use is permitted, compared to states where it is not permitted[16].

Currently, 18 states have approved the use of both medicinal and recreational cannabis, while 12 states have approved the use of CBD only in food products, energy drinks, vitamin supplements, textiles, paper, among others. A national study showed that 71.7% of patients did not report significant adverse effects associated with medicinal cannabis treatment for chronic pain[17]. The reported side effects were mild, such as somnolence (13%), dizziness (8.1%) and dry mouth (4.3%) and there were no serious adverse events requiring hospitalization or medical intervention[17].

The mechanism of action of cannabinoids shares similarities with opioids in that they require receptors located in the lipid bilayer of the cell. Both belong to the family of G protein-coupled receptors with an intracellular C-terminal and an extracellular N-terminal with seven transmembrane domains. The CB1 receptor, also known as the central receptor, is primarily distributed in the frontal cortex, basal ganglia, cerebellum, limbic system, hypothalamus, peripheral nerves, heart, vascular tissue and testes. The CB2 receptor, known as the peripheral receptor, has been found in the spleen and immune system cells, mainly macrophages, thus exhibiting anti-inflammatory effects: CB2 acts on mast cells, attenuating the release of histamine and other pro-inflammatory substances.

This case report highlights the effective control of pain and other related symptoms through the use of a balanced chemotype II medicinal cannabis formulation, administered at an optimal dose of 0.3 ml every 12 hours. This approach allowed for the successful withdrawal of a high-potency oral opioid.

These findings significantly contribute to the creation of solid evidence regarding the therapeutic effect of medicinal cannabis, as well as the presentation of a new pharmacological alternative in opioid use disorder management protocols.

Conclusion

The use of therapy with a balanced chemotype II medicinal cannabis formulation (THC 12 mg/ml – CBD 14 mg/ml) facilitated the discontinuation of a strong oral opioid regimen

with adequate pain control, reduced anxiety symptoms and improved sleep patterns. This case report reaffirms the need to generate new, higher-quality scientific evidence to promote better clinical practice related to medical cannabinoid treatments.

Author contributions

Andres Turizo Smith: Conceptualization, Investigation, Methodology, Writing–review and editing. Juan Rafael Lopez Sánchez: Project administration, Investigation, Supervision, Validation, Conceptualization, Resources, Writing–original draft and editing.

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Consent

Written informed consent was obtained from the patient for the publication of this case report. The patient also provided consent for the use of their clinical data, as detailed in Annex 1 following the References section.

Conflict of Interest

Dr. Juan Rafael López Sánchez MD acknowledges a conflict of interest as he serves as the Scientific Director of the clinic and receives honoraria from it.

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Data Availability Statement

The data and materials supporting the results or analyses presented in this study are available upon reasonable request. This research follows the Taylor & Francis Share upon reasonable request policy, which means we agree to make data and materials supporting the results or analyses presented in this paper available upon reasonable request, unless there are ethical, privacy or security concerns that prevent us from doing so. Patient personal data and identity are kept confidential in accordance with Good Clinical Practice guidelines. For additional information or data requests, please contact Andrés David Turizo Smith PhD at andturizosm@unal.edu.co or Juan Rafael López MD at +57 3107771138. For more information on data sharing policies, please visit Taylor & Francis author services.

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