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Use of cannabinoids in palliative care: an integrative review and bioethical view

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Abstract

Palliative care encompasses various measures aimed at improving patient quality of life. Among these measures, there is currently major interest in the use of cannabinoids, given their potential for symptom relief. This integrative literature review aimed to evaluate the effectiveness of cannabidiol use in palliative care. The objective was to establish a relation between the possible adverse effects and the observed benefits, in order to provide a comprehensive and unprejudiced view on its use for well-being and comfort. In addition to clinical efficacy, bioethical issues are fundamental. Respect for patient autonomy should ensure that decisions about the use of cannabinoids are informed. The principles of beneficence and non-maleficence require careful consideration of the risks and benefits. Thus, it is essential to integrate ethical considerations into the discussion on the use of cannabinoids in palliative care.

Keywords: Paliative care. Cannabidiol. Quality of life. Cannabis.

Resumo

Uso de canabinoides nos cuidados paliativos: revisão integrativa e visão bioética

Os cuidados paliativos englobam uma variedade de medidas destinadas à melhora da qualidade de vida dos pacientes. Entre essas medidas, atualmente há grande interesse pelo uso de canabinoides, dado seu potencial no alívio dos sintomas. Esta revisão integrativa de literatura tem como objetivo avaliar a eficácia do uso do canabidiol nos cuidados paliativos. Buscou-se criar uma relação entre os possíveis efeitos adversos com os benefícios observados, de modo a proporcionar uma visão abrangente e sem preconceitos sobre sua utilização para o bem-estar e conforto. Além da eficácia clínica, questões bioéticas são fundamentais. O respeito à autonomia do paciente deve garantir que decisões sobre o uso de canabinoides sejam informadas. Os princípios de beneficência e não maleficência exigem análise cuidadosa dos riscos e benefícios. Dessa forma, é essencial integrar considerações éticas na discussão sobre o uso de canabinoides nos cuidados paliativos.

Palavras-chave: Cuidados paliativos. Canabidiol. Qualidade de vida. Cannabis.

Resumen

Uso de cannabinoides en los cuidados paliativos: revisión integradora y visión bioética

Los cuidados paliativos abarcan una variedad de medidas para mejorar la calidad de vida de los pacientes. Entre estas medidas, actualmente existe un gran interés en el uso de cannabinoides, dado su potencial de aliviar los síntomas. Esta revisión integradora de la literatura pretende evaluar la eficacia del uso del cannabidiol en los cuidados paliativos. Se buscó establecer una relación entre los posibles efectos adversos y los beneficios observados, con el fin de proporcionar una visión amplia y sin prejuicios sobre su utilización para el bienestar y confort. Además de la eficacia clínica, las cuestiones bioéticas son fundamentales. El respeto a la autonomía del paciente debe asegurar que las decisiones sobre el uso de cannabinoides sean informadas. Los principios de beneficencia y no maleficencia requieren un análisis cuidadoso de los riesgos y beneficios. Es esencial integrar consideraciones éticas en la discusión sobre el uso de cannabinoides en los cuidados paliativos.

Palabras clave: Cuidados paliativos. Cannabidiol. Calidad de vida. Cannabis.

The authors declare no conflict of interest.

Research

Palliative care aims to control symptoms, as feeling happy and well is impossible when enduring pain [1]. Thus, recent years have seen a significantly increasing interest in medical cannabis in Canada, the United States (USA) and Europe, especially among patients with serious and potentially fatal diseases. This interest was supported by growing evidence of the benefits of medical cannabis for a wide range of symptoms. Recent reviews and meta-analyses have indicated advantages in the treatment of nausea, pain, spasticity, anorexia and several other symptoms [2].

Palliative care seeks to adopt a comprehensive and qualified approach to alleviate the symptoms and improve the quality of life of patients. Despite advances in medical treatments, patients under palliative care, as in advanced cancer, still suffer from significant symptoms with difficult therapeutic control. Even with the existence of a wide range of analgesics for pain control, the management of symptoms such as anorexia, fatigue and weight loss still represents a significant adversity [3]. In recent years, there has been increasing interest in the use of medicinal cannabinoids, especially for the relief of symptoms of patients under palliative care.

Cannabis contains nearly 500 bioactive compounds, including more than 70 different cannabinoids. Among them, delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD) are the predominant ones. THC, which is the main psychoactive component, acts as a partial agonist in the endocannabinoid system and may provide several benefits [3]. The most current review by the U.S. National Academies of Sciences, Engineering, and Medicine found evidence for the use of medicinal cannabinoids in intervention for some types of chronic pain, chemotherapy-induced nausea and vomiting (CINV), and spasticity in patients with multiple sclerosis, in addition to moderate evidence for sleep disorders [3]. Interest in the use of medicinal cannabinoids has increased; however, there is currently little evidence of high-quality benefits to inform health care professionals [3]. Cannabinoid products are approved for various conditions in different countries, but there is little consistency between them regarding indications and dosages, which proves the need for a more specific analysis.

This study aims to collect and analyze data in the literature on the use of CBD in clinical practice, especially by cancer patients. It will consider pharmacological and physiological aspects of the drug in the body, in addition to ethical aspects concerning its use, in order to contribute to the debate about its real effectiveness.

Method

This is an integrative literature review based on a bibliographic survey of the PubMed and Virtual Health Library (VHL) databases. Considering the proposed theme, the PICO strategy was used to initiate the research. The established question was: Is the use of cannabinoids in palliative patients effective in improving quality of life? The descriptors used were: "palliative care," "cannabidiol," "quality of life," connected by the Boolean operator "AND," filtered by the last ten years (2014–2024), in Portuguese and English. We excluded other literature reviews, articles repeated in the databases, and articles that according to the title did not address the proposed theme.

Discussion and results

Therapeutic actions

Cannabis sativa (CS) phytocannabinoids are compounds that are similar to endocannabinoids, which are molecules produced by the human body. These compounds activate the endocannabinoid system, which, through various physiological reactions, helps maintain the body's homeostasis. The literature notes the importance of the discovery of specific receptors that interact with endocannabinoids, internal substances similar to the phytocannabinoids found in the plant [4].

In a historical context, the first publications on the medical potential of cannabis were written by William O'Shaughnessy in 1839, with observations on Indian cannabis. In the 1960s, the group led by Professor Raphael Mechoulam, in Israel, isolated the components of cannabis and identified its chemical structures, providing new possibilities

for the treatment of various health conditions. In 1980, a research team led by Professor Elisaldo Carlini, at the School of Medical Sciences of Santa Casa de São Paulo, achieved a milestone by publishing a double-blind, placebo-controlled clinical trial demonstrating the anticonvulsant effects of CBD in patients [4].

It is currently known that the main psychotropic component is related to THC, while CBD is related to non-psychoactive effects. The beneficial effects of these elements range from analgesic, antiemetic, and anti-inflammatory capabilities to agents that protect the central nervous system from neurodegeneration [5]. In addition, CBD has other properties, such as antioxidant, anxiolytic and antidepressant effects [4]. In summary, peripheral CB_1 agonist drugs are used as appetite stimulants and for glandular dysfunctions; while CB_2 agonists are used in peripheral inflammation and acute pain analgesia.

Studies indicate that the effects of cannabinoids are enhanced when they are used with terpenes and flavonoids (full spectrum) and that they act in a unique manner in each individual. Even individuals with similar physiological characteristics—such as weight, height, sex, or diagnosis—exhibit varying therapeutic responses to different chemotypes or customized doses of derivatives of cannabis. This is evidence of the need for further studies on the therapeutic actions of the plant, due to its complexity and versatility [4].

Various pharmaceutical forms can be employed in the preparation of products derived from *Cannabis sativa*. The chosen route of administration affects the time of onset of effects, metabolization, and duration of active ingredients. The specific form used during treatment plays a crucial role in dose adaptation, as it directly influences the absorption and distribution of the cannabinoids present, with CBD oil being one of the most recognized forms of administration [4].

The oral route is a common route for administering medications, including cannabis oils, in tablets, capsules or liquid solutions ingested by the mouth. It is preferred when the patient is able to swallow without significant difficulties. Despite being considered safe and accessible, this route has some important limitations. The medication goes through a long path in the digestive tract and is usually absorbed only when it reaches the small intestine, where it crosses the intestinal wall and is metabolized by the liver before entering the bloodstream. This can result in a significant change in the chemistry of the medication before it reaches the site of action. Thus, the oral route is not recommended when rapid and accurate absorption of the medication is required [4].

Several patients who use cannabis prefer to inhale it, either by vaporization or by smoking (through combustion), due to the rapid absorption and immediate therapeutic effect. These forms of administration provide a bioavailability that is similar to intravenous administration, resulting in higher levels of the substance in the blood than when it is consumed orally. Vaporization is particularly popular due to its high efficacy for absorbtion of therapeutic properties of compounds present in plant trichomes, due to the precise temperature control enabled by vaporizers [4].

Main adverse effects

It is known that adverse effects are unwanted or harmful responses that occur after the administration of a medication or substance, which can vary in severity, ranging from mild and temporary to severe and permanent, and can affect any system of the body. Therefore, it is extremely important to discuss the variable adverse effects caused by the use of cannabinoids.

Katzung and Vanderah [6] provide an overview of these reactions, noting that cannabinoids can cause euphoria, dysphoria, sedation, hallucinations, xerostomia, and polyphagia. Moreover, they report that these compounds have autonomic effects on the autonomic nervous system, responsible for regulating involuntary functions of the body, such as heart rate, blood pressure, digestion and respiration. Such effects include tachycardia, conjunctival injection and orthostatic hypotension.

Casarett, Beliveau, and Arbus [2], in a retrospective cohort study based on electronic records, explored the relative contributions of tetrahydrocannabinol (THC) and cannabidiol to the management of common symptoms in palliative care. The study indicated that both cannabinoids have different physiological receptors

and responses, influencing their adverse effect profiles. THC, due to its psychoactive reactions, can cause symptoms such as anxiety, paranoia and hallucinations, in addition to euphoria. CBD does not exhibit these psychoactive effects; however, it can still cause reactions such as fatigue and gastrointestinal changes.

It is observed that the adverse effects of cannabinoids, both THC and CBD, are multiple and depend on the specific composition and circumstance of use. THC, with its psychoactive effects, presents a more complex description of risk, while CBD, although safer in psychoactive terms, is not without significant reactions. Detailed understanding of these effects is critical for the safe and effective clinical application of these compounds, especially in vulnerable populations such as pediatric cancer patients.

Use of cannabidiol in cancer

Cannabidiol is a compound that has high therapeutic capacity in several diseases, such as cancer, because, with analgesic actions, it acts as an anticonvulsant and muscle relaxant, thus alleviating some symptoms of the pathology. A study conducted by Michael Bodine and Alysia K. Kemp [7] showed that the use of this drug in cancer patients significantly interferes with the anticancer therapy of the current treatment. It was demonstrated that the use of this medication associated with immunotherapies leads to an inhibition of the proliferation of cells of the adaptive immune response, thus decreasing the efficiency of this treatment, since the power to destroy cancer cells is reduced. However, even with such proven results, some systemic symptoms of patients were also analyzed when there was THC/CBD (dronabinol/cannabidiol) supplementation together with the antiemetic regimen. These patients began to present less nausea, vomiting and pain, characteristics also noted in pediatric cancer patients, among whom nausea and vomiting were reduced by 50.6% and 53.8%, respectively.

In another study, believing in the proposal that oral cannabinoids can alliviate the symptomatic burden in cancer patients, Hardy Janet and collaborators [3] conducted a randomized, double-blind study to evaluate the efficacy of this substance in cancer patients. They studied the extent to which the use of CBD is valid, since, in some animals, the substance has shown benefits in anxiety, inflammation and neuroprotective effects. Thus, similar results were expected in cancer patients under palliative therapy. For effectiveness of this study, an analysis was performed with a control group, in which half of the participants received increasing doses of CBD, and a placebo group, in order to reach a dose that in theory would minimize the symptoms and side effects of the treatment, or that would cause an acceptable side effect in them.

Thus, a significant change was observed between the placebo group and the group receiving the drug, and the latter determined that the dose of the CBD formulation was, yes, effective, but only on determined days, on which the specific dose on that date relieved the symptoms, even with the collateral symptoms still present [3]. Therefore, it is perceived that the use of cannabinoids has great efficacy to reduce the symptomatic effects of cancer, provided they are being applied at a determined dose.

Quality of life

The use of cannabidiol for patients with diseases that affect and limit life has been shown to be beneficial for improving quality of life. A study conducted by Nimalan and collaborators [8] with 16 patients who were receiving medical cannabis for palliative care showed that cannabis use improved pain, assessed by the visual analog scale (VAS). At baseline, pain was considered severe and intense, and, after one month of drug use, it was reduced to moderate to mild; after three months of use, pain was considered mild. In addition, with pain relief, there was an improvement in mobility and in the depressive and anxious condition of the patients. However, this same study showed that medical cannabis can have adverse effects such as lethargy, ataxia and dysgeusia.

Another study, carried out by Alexandra Smith and collaborators [9], on well-being and medical cannabis, showed that patients in palliative care, especially cancer patients, were willing to use cannabis even with adverse effects, as they reported that the benefits of using cannabidiol

in improving quality of life outweigh the adverse effects they could suffer.

Bioethical view

Principlist bioethics is founded on a framework of principles that situate the human being at the center of ethical concerns. Among these principles, the following are notable: beneficence, which seeks to promote well-being; non-maleficence, which aims to avoid harm; autonomy, which values and respects the individual's capacity to make decisions about their own life; and justice, which guarantees equity in access to resources and treatments [10].

In the context of the use of cannabidiol in clinical practice, it is essential to consider, first of all, respect for patient autonomy. According to a study carried out by Abreu and collaborators [11], when the patient has adequate conditions of judgment, the health care team must clarify the situation and take their opinion into consideration. Shared decision-making is a central process in this scenario, in which the physician plays the fundamental role of explaining risks and benefits in a clear and accessible manner, deliberating on them together with the patient.

In addition, although medical evaluation and indication are essential, understanding the wishes, desires and expectations of both the patient and their family contributes to the construction of a human-centered practice. This approach not only improves the quality of life, but also ensures that medical conduct is guided by respect for the patient's dignity and individual values. In considering the use of cannabidiol, it is equally important that the health care team adopts a posture that is sensitive and open to cultural, religious, and social differences that can influence perceptions and decisions about treatment. Recognizing these influences enables building a relationship of trust and ensuring that the provided care is inclusive and adapted to the specific needs of each individual.

Final considerations

The study of the effects of cannabidiol on patients in palliative care shows both risks and benefits. THC can cause psychoactive effects, while CBD can have adverse effects, but its benefits—such as pain relief and improved emotional well-being through anxiolytic effect—are significant for cancer patients; this fact shows the need to consider the patients' individual characteristics, so the benefits outweigh the risks, individualizing its use.

The increased use of CBD to treat symptoms such as anorexia, fatigue and pain demonstrates its therapeutic potential, although it faces ethical, social and religious barriers, hindering not only its applicability in practice, but also the formulation of new clinical studies to assess the safety and efficacy in human beings. Thus, it is clear the need for further studies to define the role of CBD in medical practice and optimize its administration, especially on the best dosage, formulation and route of administration, always individualizing the treatment for each patient and focusing on providing a better quality of life.

Regarding the bioethical view, CBD use in palliative care shows the importance of integrating the principles of beneficence, non-maleficence, autonomy and justice into patient care. Respecting patient autonomy, promoting shared decisions, is fundamental to ensure that the treatment is aligned with their values and desires. In parallel, rigorous risk and benefit assessment strengthens the ethical commitment toward avoiding harm while seeking to promote well-being. By integrating these perspectives of ethics, assessment and inclusion, CBD use can be consolidated as a practice that is not only clinically effective, but also ethically responsible, providing a humanized and compassionate approach to patients in situations of vulnerability.

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Participation of the authors

Thamirys Andrade Ferreira de Oliveira Ribeiro participated as a researcher and advisor in all stages of the study. All other authors searched the indexed databases. Ana Flávia Espindola reviewed the text and was responsible for drafting the discussion on therapeutic actions, in addition to developing the methodology. Bruna Medeiros Gomes was responsible for drafting the discussion on the use of cannabidiol in cancer. Jéssica de Brito Barroso was responsible for drafting the discussion on quality of life. Mariella Gahyva Munhoz Figueiredo was responsible for drafting the introduction. Karina Silva Angelo was responsible for drafting the discussion on therapeutic actions and the final considerations. Helena Luiza Bez Batti Teles also reviewed the text and was responsible for drafting the discussion on the main adverse effects.

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