Challenges of the greater use of cannabinoids in palliative care

Raíssa Alves dos Santos[a], Ricardo Manoel de Armada Maturana[b].

[a]Escola de Medicina Souza Marques, Faculdade Souza Marques, Rio de Janeiro, Brazil, rah.alves07@gmail.com.

[b]Escola de Medicina Souza Marques, Faculdade Souza Marques, Rio de Janeiro, Brazil, ricmaturana@gmail.com.

Abstract. Cannabis has been used over the years for healing and as a mind-altering drug. The expansion of cannabinoids in palliative care is leading to changes in legislation in many countries therefore permitting greater use of this substance prescribed for extended indications including palliative care, intractable epilepsy, chronic pain, chemotherapy-induced nausea and vomiting (CINV), and many other symptoms. This study is a literature review that aims to deliberate on the restrictions of the greater use of cannabinoids in patients who need palliative care. The research process for this study occurred in August 2023 and consisted of a search on the database platforms PubMed and Scholar Google using the keywords 'Medical cannabis', 'palliative care', 'cannabinoids', and 'review'. The logical operators were also used for more precise results. Although the number of prescriptions of medicinal cannabinoids supplied by physicians is increasing such as the number of publications about the use of cannabinoids in palliative care, the evidence supporting it is still limited. This study aims to discuss the challenges of the use of cannabinoids in patients who need palliative care.

Keywords. Medical cannabis, palliative care, cannabinoids, review.

1. Introduction

In Chinese Medicine, the use of cannabis started nearly 5000 years ago serving as a healing and mind-altering drug just like nowadays. Over time it became a prosperous trading and in the present day, cannabinoid use has expanded especially for medical reasons. The proportion of cannabinoids differs depending on the origin of the plant (where it has been cultivated), but the main and most well-known of these are delta- 9-tetrahydrocannabinol (Δ9-THC) and cannabidiol (CBD) (Turgemand et. al 2017).

Cannabinoids stimulate the endogenous cannabinoid system by altering levels of endocannabinoids (eCBS). Those substances induce physical and mental effects by binding to G protein-coupled cannabinoid receptors 1 and 2 (CB1 and CB2) that are extensively distributed throughout the human body, with the highest concentration of CB1 and CB2 found in the central nervous system and immune cells correspondingly. Derived from arachidonic acid, eCBS are neuroactive lipid messengers involved in physiological processes like reward, motivation, memory, learning, and pain processing (Turgeman et al. 2017).

Presently there is increasing interest in the use of medical cannabis for the relief of symptoms in palliative care patients. This conjecture is leading to changes in legislation in many countries such as Australia, the UK, the USA, and Israel, thus permitting greater use of the cannabinoids prescribed for extended indications including palliative care, intractable epilepsy, chronic pain, spasticity associated with multiple sclerosis, and chemotherapy-induced nausea and vomiting (CINV) (Good et al. 2019).

Although the number of prescriptions of medicinal cannabinoids supplied by physicians is increasing, as is the number of publications about the use of cannabinoids in palliative care, the evidence supporting it is still limited. The exact constitution of most of the 'medicinal cannabis' used by the general population is generally unknown because a small proportion of users obtain cannabis through legal ways. On top of that clinicians are still uncertain about the specific compounds within the cannabis plant that are most efficient for individual symptoms. There are also concerns to be elucidated about the interaction with other medicines, especially in elderly people and children. Another issue is the unexplored adverse effects that medicinal cannabis may cause. All these problems interfere with the

process of construction of scientific evidence (Herbert et al. 2021). This study aims to discuss the challenges of the use of cannabinoids in patients who need palliative care.

2. Methodology

After the analysis of the main subject and the possible approach, this study aims to investigate and discuss the obstacles involved in the use of cannabinoids in palliative care. The hypothesis is that medical cannabis is largely used for many symptoms but the specific application for its use is still vague therefore more research work is needed.

The investigation process for this study occurred in August 2023 and consisted of a search on the database platforms PubMed and Scholar Google using the keywords 'Medical cannabis', 'palliative care', 'cannabinoids', and 'review'. The logical operators were also used for more precise results. The chosen articles respected the inclusion criteria formed by the factors: complete structure, majority of recent publications (2001-2023), and published in English, totalizing 6 (six) published articles.

This study is a literature review that aims to deliberate on the restrictions of the greater use of cannabinoids in patients who need palliative care. The hypothesis is that medicinal cannabinoids contribute positively to controlling symptoms in palliative care.

The primary objective is to inspect the utilization of the current application of medical cannabis in patients in palliative care and to observe the effects of its use. Secondary objectives are to establish the implications that hamper the largest use of medical cannabis in palliative care.

3. Results

Table. 1 - **Worldwide distribution of legalized medical cannabis.**

Continents	Number of countries where medicine cannabis is legalized	Countries per continent	Percentage Of Total
Africa	9	54	16,66%
America	15	35	42,85%
Asia	6	48	12,5%
Europe	32	47	68,08%
Oceania	2	16	12,5%
Total	64	200	32%

Source: UNODC, World Drug Report 2022 (United Nations publication, 2022).

As can be observed, Table 1 shows the number of countries in each continent where medicinal cannabis is legalized. According to the data, Europe is the continent that has the highest percentage of countries where medicinal cannabis is legalized (68,08%), followed by America, which shows a percentage of 42,85% of countries where medicinal cannabis is legalized.

Countries from Africa, Oceania, and Asia showed similar results on their data, 16,66%, 12,5% and 12,5%, respectively. The world average is 32% of countries of Earth, considering the evaluation of a total of 200.

4. Discussion

After the results showed, the percentage difference in medicinal cannabis legalized in each continent can be observed. The main difference in the number of countries per continent occurs thanks to countless factors, but it is necessary to highlight that the cultural singularities between distinct nations and their government rules impact the legalization of the medicinal drug. It is notorious that continents with more liberal governments present higher countries percentages where medicinal cannabis is legally used. However, in places where conservatory management forms are more prevalent, a lower percentage of countries that legalize medicinal cannabis is seen.

Moreover, although there is a necessity for a higher number of studies and reliable database information about the theme in question, it seems the main problem of the use of cannabinoids, including medicinal use, is that this is treated under the vision of prejudice by a huge part of the world population. The prejudgment occurs due to several causes, but an

important root of this problem is the association between recreational users and their stigmatized behavior. Therefore, people must know the difference between the recreational use of cannabis and the application of medicinal cannabis in Medicine, especially for palliative care, which is such an important field of use, owing to the shown benefits.

In addition, is important to keep in mind that Cannabis has been used for over the years as an analgesic and some studies suggest its strong therapeutic adjunct, for relieving neuropathic pain because thinking that way people can understand that it used to be used like any other medicament. In the UK, a commissioned review determined that there was good evidence for its use in chronic non-cancer pain, spasticity, CINV, and anxiety, with moderate evidence for use in chemotherapy-induced anorexia, sleep disorders, post-traumatic stress disorder, fibromyalgia, and Parkinson's disease symptoms. Even with these applications shown in studies, it is suggested that much more investigation and proper research (Clinical trials) are needed. Likewise, it is important to show that in cancer therapy many patients use cannabis believing in its anticancer effects, but this hasn't been demonstrated (Herbert et al. 2021).

In Pediatrics, some studies demonstrated reasonable evidence that medicinal cannabis, specifically CBD, is effective for children with treatment for refractory epilepsy. In 2017 a systematic review study by the American Academy of Pediatrics (AAP) did not recommend the use of medical cannabis in children outside the FDA (Food and Drugs Administration), which diverges from clinical practice, where cannabis therapy is used in harsh debilitating circumstances. Also, a German study discovered an affirmative response to synthetic THC (dronabinol) in children with dystonia and spasticity, another example of neurological conditions (Herbert et al. 2021).

The antiemetic and nausea effects have been demonstrated using THC, its synthetic analogs, and CBD. One systematic review by Tramer et. al investigated 30 randomized comparisons of cannabis with placebo or antiemetics. It was inferred that in all 1366 patients involved in the review, the cannabinoids were found to be substantially more efficient antiemetics than prochlorperazine, metoclopramide, chlorpromazine, thiethylperazine, haloperidol, domperidone, or alizapride. Additionally, cannabinoids were shown to be potential backup drugs in cases where other antiemetic therapy options have proved unfitting. This pharmacological property occurs due to the action of cannabinoid substances acting on their very own receptors, guaranteeing them a different mechanism of action from those of ordinary antiemetics (Mikolajczak et al. 2018).

Furthermore, healthy professionals must be updated about the theme to administer the medicine in the indicated way, respecting the individuality of each patient and suggesting the best treatment for each one. It is really important to observe the adverse effects such as somnolence, dizziness, dry mouth, and disorientation, as well as euphoria, anxiety, and hallucination. Problems with memory and cognition, addiction, depression, and anxiety disorders have also been related to cannabis use; those events are mostly associated with Δ9-THC. Recreational cannabis, used in the streets notably contains different levels of medicinal cannabis supplied for research or patient use and then the effects and consequences found will differ (Turgeman et al. 2017).

The long-term work that needs to be done is to demonstrate to patients and the general population that cannabinoids and their derivatives (THC and CBD) are drugs like any other and fantastic benefits were shown in the most diverse areas and diseases if they were used by the right way (Turgeman et al. 2017). Nevertheless, it is also important for more research to identify more collateral or bad effects on human beings and their organisms.

Finally, it is important to show some limitations of the present study. Readers have to keep in mind that a problem with the results is that the total number of countries in the world is different depending on which databases are used, so it is always necessary to catch up with official information, such as the United Nations website and trustworthy articles. Another implication is that some countries have federation states with different levels of autonomy, for example, two extremes: the United States of America and China, the first with more state autonomy and the second without it. This characteristic needs to be in the reader's mind because, having the example of the USA, it is not always the best option to generalize all states of the USA in one result, because they have different laws about the theme. However, in this case, for best data analysis, the entire country is considered by the option of the majority states.

Another limitation is that, usually, governmental databases are not reliable thanks to the scarcity of research about cannabis epidemiology, occurring to paucity of funds and other causes.

5. Conclusion

The positive impact of medical cannabis is undeniable, especially in palliative care providing comfort and dignity at the end of life. However, the need for deeper studies such as clinical trials and cohort studies is evident. These studies are indicated to solve the questions that are yet without answers, like the specific cannabinoid compounds indicated for individual symptoms, the drug interactions that are still unclear, and the risks of the use of medicinal cannabis in different stages of chronic diseases. The medicinal interactions are numerous but the clinical

evidence of these is undiscovered, interactions with other medications should be meticulously supervised (Herbert et al. 2021).

Therefore, basic clinical trials are recommended to determine and further investigate the right constellation of drug composition, dose, and means of administration, to indicate specific cannabis-based medicine per indication and patient. The guidance for the use of medicinal cannabis should be constantly updated and reviewed to reduce the risks and potential complications in patients with delicate health conditions. With advances in legislation, appropriate training and education for health professionals and a higher number of cannabinoid studies the treatment protocols and guidelines could change and benefit more patients in palliative care (Turgeman et al. 2017).

6. References

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