

USE OF CANNABIDIOL IN THE TREATMENT OF PATIENTS AFFECTED BY CEREBROVASCULAR ACCIDENT

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INTRODUCTION

Stroke is termed in the literature as a clinical condition that provides the patient with a sudden illness that immediately causes a cessation of blood flow to the brain, evidenced by ischemia or bleeding that can lead to serious neurological damage, partially or fully compromising the patient's quality of life (MANIVA *et al.*, 2018). Stroke can be characterized as an obstruction of a blood vessel in the brain called ischemic stroke, or as a cerebral hemorrhage that is hemorrhagic stroke (MARTINS, *et al.*, 2019).

Worldwide, stroke is the second determinant among deaths, especially in adults and the elderly. In recent years, in Brazil, the numbers of affected patients are worrisome, since numbers are presented that exceed 160,621 hospitalizations with a morbidity rate that exceeds 51.8% (LIMA *et al.*, 2016).

The American Heart Association (2012) determined that stroke causes extensive damage to patients that can recur in a second attack if there is no quality follow-up. The association makes it clear that, every 4 hours, an individual dies as a kind of a result of cardiovascular problems, second only to cancer (ROGER *et al.*, 2012).

In its pathophysiology, stroke shows a considerable drop in the amount of adenosine triphosphate (ATP), offered by ischemia, which leads to a decrease in its production levels. Another factor observed is the occurrence of an increase in the levels of lactic acidosis which, in turn, causes an ionic imbalance in the neurons. This mismatch impairs the function of neurotransmitters, contributing to their increase and failure in reception, such as glutamate. The excessive amount of glutamate causes excitotoxicity through NMDA and AMPA receptors and calcium, generating an unusual deposit in the catabolic pathways of proteases, lipases and

nucleases, increasing the chances of triggering brain edema (RODRIGUES; SANTANA; GALVÃO, 2017).

The modifiable stroke factors are recognized in the literature as: systemic arterial hypertension, atrial fibrillation, diabetes mellitus, smoking and dyslipidemia. All bad habits of life lead the individual to a risk situation before the stroke. Therefore, it is necessary to educate the population about the risks of conditions such as obesity, physical inactivity and tobacco use so that modifiable risks are minimized (LUIZ *et al.*, 2021; MARIANELLI; MARIANELLI; NETO, 2020).

According to data from the study by Pereira (2013), patients who survived after a stroke exceed the two million mark; however, about 40% of them remained with permanent sequelae that cause a deficit in their daily occupations. These cases range from taste damage to those that completely deprive the victims of their autonomy.

Regarding the most evident sequelae in patients with stroke, it was observed that 23 professionals responded that they observed more motor skills (92%), 22 balance and coordination (88%), 18 behavioral and emotional (72%), speech (68%), sensitivity (44%), 8 taste (32%), 4 interpretation (16%), 3 vision (12%), 3 others (12%), and 2 hearing (8%) (ALVES; PAZ, 2018 p. 26).

In this context, the nursing professional has attributions that start from the prevention of cases in Basic Health Units (UBS), performing individual and collective interventions that aim at the adoption of healthy habits that remove the risk of cardiovascular situations, especially the stroke. Nurses must have their knowledge focused on strategies that welcome the community, preventing individuals from reaching critical levels for hospital care (BRASIL, 2013).

In the midst of such a devastating pathology that must be known intimately by nursing

professionals, cannabidiol emerges through research to be analyzed as an adjunct in the treatment of patients affected by stroke. This substance is extracted from *Cannabis sativa* - popularly known as marijuana (MURKAR *et al.*, 2019). Cannabidiol does not have the psychoactive effects that marijuana induces, such as agitation and hallucinogenic effects, they interact directly with the cellular receptors of the immune system, offering benefits listed in recent studies, mainly at neurological levels. In other systems, cannabidiol has great relevance for the treatment of refractory pain, where other conventional therapies have been used and have not been successful (BRUCKI *et al.*, 2015).

Brazil (2015) defines that patients who underwent a study with the use of Cannabidiol reduced about 50% of daily epileptic seizures in children with chronic seizures, those who are diagnosed with acute seizures, the result reached even higher rates.

In the study by Escobar (2018), Δ^9 -THC and CBD, found in Cannabidiol, have properties that modify cognitive and motor action that can act in depressive states. However, Δ^9 -THC has psychoactive ramifications that still have limitations in its study. Even though it is a subject of complex understanding, ANVISA released substances extracted from Cannabidiol so that the studies could be carried out in the national territory.

Cannabidiol as a medicinal use has been gaining prominence in science for a few years now. This substance demonstrates important advances in the field of health, even though it is the subject of much controversy in the legal view, because in Brazil, marijuana is considered a prohibited narcotic in its commercialization. In view of all this progress, the study becomes relevant because it asks whether cannabidiol would

be a medication of choice to improve the quality of life in stroke patients?

For the academic world, research becomes relevant as it enters an innovative and promising environment that can expand the horizons of nursing professionals so that knowledge in this area becomes increasingly accessible and contributes to the quality of life of patients. and understanding of students in the area.

Thus, the objective of this study was to report, through the literature, the possible benefits of the use of cannabidiol, to relate them to the sequelae caused by the Cerebral Vascular Accident, and to bring evidence that the use of the substance contributes to the improvement of the quality of life of the patients. patients.

METHODOLOGY

The method used was the integrative literature review, which aims to describe the data from the literature presented, basing a study relevant to nursing (SOUZA, 2010). To proceed with the integrative review, it was necessary to follow the steps that define the search and understanding of the data:

- Construction of the guiding question: would cannabidiol be a medication of choice to improve the quality of life in stroke victims?
- Search for samples: article from the last 10 years of the SciELO database (3) + MEDLINE (3) + PUBMED (10), + TECHNICAL STANDARDS AND LEGISLATIONS (2) the following descriptors “CVA”, “CVA Treatment”, “Rehabilitation”, “Cannabidiol”, “Care and Quality of Life”. The inclusion criteria were: QUALIS Capes factor from A1 to B4. The Qualis classification is the evaluation of academic publications, adding quality to scientific content and ranking the journals (LEITE;

CODATO, 2013). Also included were articles in Portuguese, English and Spanish whose texts are complete, theses, dissertations, monographs and papers from congresses and scientific weeks were excluded, as well as articles whose type of study were systematic or literature reviews;

- Data collection: a systematic framework was created for the insertion of articles that answer the guiding question;
- Extraction of information: systematic reading, followed by discussion of the results;
- Discussion of selected results: resulted in the analysis of all articles and their appropriate narratives; presentation of the integrative review.

RESULT

To answer the guiding question, it was possible to search for articles that analyzed the topic, respecting the selected descriptors, as well as the inclusion criteria set out in the methodology.

After inserting the studies in Table 1, it was possible to view the articles by publication date, and through the study it was observed that over the last five years the subject in question was often the object of research.

The articles arranged in the results item demonstrate that the analysis was carried out through recent studies with a predominance of the years 2021 to 2017, not exceeding ten years of publication as exposed in the methodology. Recent research demonstrates the true scenario of the chosen theme, as well as demonstrates the number of published studies.

Evidence from a study classifies the relevance of selected articles, according to their impact in the scientific field. The entire path to be followed by researchers is extremely important to obtain reliable studies

in internationally recognized search bases. Therefore, it is necessary that the analysis be judicious so that the reader can have access to a critical and reliable text. The studies selected by the authors must be included in the levels of evidence and be consistent with clinical practice in health. All attached studies must provide the reader with accurate information that contributes to public health (SAMPAIO; MANCINI, 2007). As shown in table 2, six studies were included in the category of level IV, four in level I and three in level II.

As for the quality level of the articles, the Qualis grade represents the evaluation of national and international journals referring to A1 and A2 - International Excellence, B1 and B2 - National Excellence, B3, B4 and B5 - Medium Relevance, C - Low Relevance. Of the 18 articles, 56% are graded A1, followed by 28% B4, 5% B2 and B2; and 6% B3.

DISCUSSION

In this section, the results of the authors attached in Table 3 will be discussed in order to answer the guiding question. The well-being of patients who received Cannabidiol was discussed in the analyzed articles. It is possible to emphasize that there is a scarcity of national articles that talk about the benefits of Cannabidiol in patients who have suffered a stroke, and it is possible to provoke more studies in the area so that patients can gain more and more benefits in the treatment of sequelae.

MEDICINAL USE OF CANNABIDIOL IN BRAZIL AND IN THE WORLD THROUGH THE INCIDENCE OF CVA

The use of Cannabidiol for medicinal purposes has been carried out for more than 4 thousand years before Christ, in records of attacks such as convulsive crises, labor, bites of venomous animals and malaria. This entire process was carried out by individuals who

Article title	Author	Magazine	Year	Level of Evidence / Qualis	Kind of study	Main causes identified in the article	Main goal
Physiotherapy and Functionality in Post Covid19 Patients: Literature Review	Oliveira <i>et al.</i> ,	Higia - Journal of Applied Health and Social Sciences of the West of Bahia	2021	IV/B4	integrative review	Risk of venous and arterial thromboembolism after covid-19, including stroke with its cognitive and physical deficits	Evaluate scientific evidence on physiotherapy and functionality in post-covid-19 patients and identify main functional changes secondary to this disease.
Epidemiological profile of patients with ischemic stroke undergoing thrombolytic therapy: an integrative review	Roxa <i>et al.</i> ,	Brazilian Journal of Development	2021	IV/B2	integrative review	Among the main risk factors for stroke, systemic arterial hypertension (68.9%), dyslipidemia (29.8%), diabetes mellitus (26.7%) and heart disease (22.7%) were perceived., smoking (62.5%).	To analyze the epidemiological profile of individuals with ischemic stroke who obtained thrombolytic therapy (TT).
Cannabinoids In Neurology - Position Paper From Scientific Departments From Brazilian Academy Of Neurology	Bruck; Meadow	Brazilian Academy Of Neurology	2021	II/A1	documentary study	<i>Cannabis</i> extract may be a therapeutic resource for neuropathic pain syndrome	To describe the evidence for the medical use of cannabidiol in the literature
Medicinal cannabinoids to alleviate the burden of symptoms in palliative care of patients with advanced cancer	hardy <i>et al.</i> ,	Essay	2020	I/B3	Randomized clinical trial	Improves pain, diarrhea and appetite levels	To analyze the use of Medicinal Cannabinoids for Symptom Relief in Palliative Care of patients with advanced cancer
Oral medicinal cannabinoids to relieve symptom burden in the palliative care of patients with advanced cancer: a double-blind, placebo controlled, randomized clinical trial of efficacy and safety of cannabidiol (CBD)	Good <i>et al.</i> ,	BMC Palliative care	g 2019	I/A1	Randomized clinical trial	The combination of tetrahydrocannabinol and cannabidiol may contribute to sleep maintenance	To define the role of cannabidiol (CBD) in managing symptom burden in patients with advanced cancer in standard palliative care.

Cardiovascular risk in patients with Inflammatory Bowel Disease.	Goncalves; Nunes	Journal of Family Medicine and Mental Health	2019	IV/B4	integrative review	Inflammatory bowel disease impairs natural intestinal and systemic functions that can be found in the literature as a predisposing factor for stroke, Crohn's disease and ulcerative colitis.	To associate ischemic bowel disease with cardiovascular risk and the impact of treatment during the period of disease activity.
Cannabinoids and the expanded endocannabinoid system in neurological disorders	Cristino <i>et al</i>	Nature reviews neurology	2018	I/A1	Randomized Clinical Study	Cannabidiol showed protection against stroke IN preventing the rupture of veins, attenuation of cerebral edema	discuss engagement and clinical relevance of the endocannabinoid that for a variety of neurological disorders.
Effect of medical cannabis on thermal quantitative measurements of pain in patients with Parkinson's disease	Shohet	European Journal of Pain,	2017	IV/A1	Quantitative study	Motor functions and pain symptoms were decreased after the use of Cannabidiol in the surveyed samples	To evaluate the effect of cannabis on motor symptoms and pain parameters in patients with Parkinson's disease (PD).
Cannabinoids for Treating Epilepsy in Children	Trinity	unit	2017	II/B4	documentary study	Cannabidiol can reduce seizures leading to more safety and quality of life	Explore the scientific evidence on the use of cannabinoids for the treatment of epilepsy.
Neonatal Ischemic Stroke in the National Registry of the Pediatric Surveillance Unit: How Are These Children Six Years Later?	Fraga; Monteiro	Portuguese Pediatric Act	2017	IV/B4	Prospective and descriptive cohort study	Stroke This type of event can generate perinatal brain damage, leading the baby to neurological and cognitive deficits throughout his life.	To evaluate the cases of symptomatic CVA reported in the pediatric surveillance unit (PSU) in Portugal between 2009-2011 and the respective long-term follow-up.
Micropropagation of Cannabis sativa L.—An Update	can <i>and et al.</i> ,	springer	2017	I/A1	randomized clinical trial	There are records of studies with the use of marijuana for more than 4 thousand years with attacks such as convulsive crises, labor, bites of venomous animals and malaria.	Address current applications of modern biotechnology in the propagation of elite cannabis plants.

The current status of artisanal cannabis for the treatment of epilepsy in the United States	Sulak <i>et al.</i> ,	Elsevier	2017	IV/A1	Descriptive retrospective cohort study	It was only in the 1990s that the medicinal use of Cannabis regained the interest of scientific society, after the discovery of the Endocannabinoid and its CB1 and CB receptors.	Discuss clinical considerations, including potential risks and benefits, challenges related to artisanal preparations, and cannabinoid dosing.
The incidence of pregnancy-related stroke: A systematic review and meta-analysis	Swartz <i>et al.</i> ,	sage journals	2017	IV/A1	Systematic review and meta-analysis	Stroke can cause irreparable consequences in its victims due to the signs and symptoms presented, such as loss of function in the focal portion of the brain.	To assess the incidence of stroke during pregnancy and the puerperium.
The use of cannabidiol in the treatment of epilepsy	Matos <i>et al.</i> ,	Chemistry Virtual Magazine	2017	IV/B4	integrative review	The commercialization of Cannabis has also been carried out for a long time, but after the industrial revolution	To gather bibliographic data that describe the therapeutic profile of cannabidiol (CBD), the main non-psychoactive component of the Cannabis sativa plant (marijuana), in the treatment of psychic disorders, especially in refractory epilepsies.
Cannabinoids in neurology – Brazilian Academy of Neurology	Bruck <i>et there</i>	Arch. of Neuropsychiatry	2015	II/A1	documentary study	Cannabidiol does not have the psychoactive effects that marijuana induces, such as agitation and hallucinogenic effects, they perform a direct interaction with cellular receptors and	Analysis the use of cannabidiol in some neurological conditions was released by the CRM of São Paulo and by ANVISA
Neuroplasticity in the rehabilitation of stroke patients spastic	Zilli, Lima, Kohler	Journal of Occupational Therapy of the Federal University of São Paulo	2014	IV/B1	integrative review	Patients who suffer stroke are at risk of spasticity, a condition that leads the individual to episodes of constant involuntary movements.	To analyze the beneficial results of studies based on the principle of neuroplasticity as a rehabilitation mechanism in patients with spastic stroke.

Stroke and pregnancy: clinical presentation, evaluation, treatment, and epidemiology	Grear <i>et al.</i> ,	Wolters Kluwer	2013	IV/A1	integrative review	Emergency care: arteriosclerotic pathology; embolisms; presence of hypotension; thrombus	Discussion of the symptoms and clinical presentation of stroke is provided and current guidelines for the treatment of stroke in pregnancy.
A placebo-controlled, parallel-group, randomized withdrawal study of subjects with symptoms of spasticity due to multiple sclerosis who are receiving long-term Sativex® (nabiximols)	notcutt <i>et al</i>	multiple Sclerosis Journal	2012	I/A1	randomized clinical trial	Improved spasticity of patients	To assess the maintenance of Sativex efficacy in subjects who have achieved long-term symptomatic relief of multiple sclerosis (MS) spasticity and to assess the impact of sudden drug withdrawal.

Table 1- Studies analyzed.

Source: prepared by the authors (2022).

Level of evidence	Kind of study	Number of articles	total percentage
Level I	randomized clinical trial	5	27.8%
Level II	documentary study	3	16.7%
Level IV	Integrative review/ Prospective and descriptive cohort study/ Quantitative study	10	55.5%
Total:	-	18	100%

Table 2- Types of studies.

Source: prepared by the authors (2022).

took care of the health of the population at the time through teas and supplies called dressings (LATA *et al.*, 2017). The commercialization of Cannabis has also been carried out for a long time, but after the industrial revolution, it was seen as a curative input for pathologies that involved sleep and the need for sedation. In 1930, the use of the substance evidenced a discussion due to the effects observed in the public who used the substance (MATOS *et al.*, 2017).

When studies were developed, the substance chloral hydrate, barbiturates and paraldehyde, the compounds that led patients to unwanted situations, was evidenced (SULAK *et al.*, 2017); It was only in the 1990s that the medicinal use of Cannabis aroused the interest of scientific society again, after the discovery of the Endocannabinoid and its CB1 and CB2 receptors that act directly on chronic pathologies linked to the nervous system (OLIVEIRA *et al.*, 2021). U

Stroke can cause irreparable consequences in its victims due to the signs and symptoms presented, such as loss of function in the focal brain portion, which, in many cases, can present with neuronal damage. Patients who are admitted to urgent and emergency services in Brazil are affected by findings such as: a) arteriosclerotic pathology; b) embolisms; c) presence of hypotension; d) thrombi (SWARTZ *et al.*, 2017; GEAR *et al.*, 2013).

As for the non-modifiable risk factors for the onset of stroke, they include race, geographic location, genetics that induce predisposition and age. With the increase in life expectancy of the Brazilian population, an increase in chronic pathologies was also observed. Through this data, it is necessary to create public health actions to remove individuals from the mortality risk range (MARIANELLI; MARIANELLI; NETO, 2020).

IMPROVEMENTS IN QUALITY OF LIFE

Patients who suffer stroke are at risk of spasticity, a condition that leads the individual to episodes of constant involuntary movements due to damage to the central nervous system (ZILLI; LIMA; KHOLER, 2014).

In the Notcutt study *et al.*, (2012), after inserting the compound *Sativex*, derived from marijuana to patients suffering from spasticity, improvements in involuntary movements were identified. After 12 months of studies, the samples that received the input showed improvement “in the objective scales for measuring spasticity”, demonstrating positivity in the treatment of a sequela of the nervous system.

A very common neurological sequelae in patients is central neuropathic pain, which starts in the central nervous system a few days after the stroke. The syndrome can generate pain throughout the body, leading the patient to constant suffering (RAMOS; PINA, 2021).

In the study by Bruck *et al.*, (2015), the results of the analyzes are still conflicting, however, the published data demonstrate that the *cannabis extract* can be a therapeutic resource for the syndrome, when the patient no longer responds to traditional methods.

In the study by Shohet (2017), motor functions and pain symptoms were decreased after the use of Cannabidiol in the surveyed samples. Patients suffered from a low quality of life before the implementation of the study, but with the improvement of the determinants, the pain rating questionnaires and visual analogue scale and *Unified PD Rating scale* demonstrated success in daily activities, considering the beneficial input in this segment.

Hemorrhagic stroke can cause victims numerous daily convulsions due to ischemia of nerve cells and brain hemorrhage, as found in the literature. These seizures can decrease

the quality of life of patients because they happen constantly (ROXA *et al.*, 2021). In the study by Trindade (2017), cannabidiol can reduce seizures, leading to more safety and quality of life in both adults and children who resisted treatment with standardized medications.

In premature babies, neonatal ischemic stroke (NCACV) occurs on a considerable scale in the country's Neonatal Intensive Care Units, especially in premature babies. This type of event can generate perinatal brain injury, leading the baby to neurological and cognitive deficits throughout his life. AVCIN is evidenced by a vascular "insult" in the arterial focus around 28 weeks of gestation (FRAGA; MONTEIRO, 2018).

In the study by Marques and Almeida (2012), cannabidiol presented protection against CVA, preventing the rupture of veins, attenuation of cerebral edema. The authors describe cannabidiol as a protector against transient or permanent rupture of the cerebral artery.

Inflammatory bowel disease (IBD) is diagnosed in several patients who have had a stroke or are at risk according to the study by Gonçalves and Nunes (2019), the chronic pathology impairs the natural intestinal and systemic functions that can be found in the literature as a predisposing factor for stroke, Crohn's disease and ulcerative colitis. The authors state that IBD has a direct link with the formation of venous thromboembolism, coronary artery disease and stroke.

To Hardy *et al.*, (2020) Cannabidiol improves the sensation of pain, diarrhea and appetite levels, as exogenous cannabinoids increase the feeling of well-being of the aforementioned symptoms. The authors also mention that the substance can act as an anti-inflammatory in IBD patients, considered beneficial for the quality of life of the analyzed samples.

The presence of insomnia is reported in some stroke patients; the involvement causes sleep disturbance, which can lead to other pathologies and the use of more drugs to improve the quality of life. The combination of tetrahydrocannabinol and cannabidiol can contribute to sleep maintenance, as the analyzed samples showed greater drowsiness, stating that the union of the two compounds can contribute to sleep hygiene (GOOD *et al.*, 2019).

FINAL CONSIDERATIONS

It is concluded that, through the literature, there are clear evidences that the use of Cannabidiol in the treatment of sequelae caused by stroke contributes to improving the quality of life of patients in several aspects. It was possible to verify in the midst of the analyzes that there is a shortage of studies that exclusively analyze the benefits of Cannabidiol related to stroke. Therefore, the present study provokes new field studies so that the evidence is published so that patients can gain a better quality of life.

It is worth mentioning that the nurse is a precursor of health and must act in the prevention of disease at the levels of health care, contributing to the reduction of cases and, consequently, raising the levels of quality of life of the population. The same has autonomy to formulate strategies that serve the entire community, including men and women in preventive programs that take care of the presented theme. As for studies with Cannabidiol, nurses must also participate so that society has access to innovations that can lead to good results for those who need it most.

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