Use of cannabinoids in the treatment of persons with Alzheimer

Uso dos canabinóides no tratamento de pessoas portadoras de Alzheimer

Uso de cannabinoides en el tratamiento de personas con alzheimer

Yara Paiva Bittes[1], Leila Batista Ribeiro[2], Gleisiane Silva Anselmo[3], Taynara Câmara Lopes Dantas[4], Marcus Vinícius Ribeiro Ferreira[5], Wanderlan Cabral Neves[6], João de Sousa Pinheiro Barbosa[7], Danielle Ferreira Silva[8]

How to cite: Bittes YP, Ribeiro LB, Dantas TCl, Ferreira MVR, Neves WC, Barbosa JSP, et al. Use of cannabinoids in the treatment of persons with Alzheimer. REVISA. 2021; 10(Esp.2): 887-98. Doi: https://doi.org/10.36239/revisa.v10.nEsp2.p887a898

1. Planalto University Center of the Federal District. Brasília, Distrito Federal, Brazil. https://orcid.org/0000-0002-5360-6984

2. Planalto University Center of the Federal District. Brasília, Distrito Federal, Brazil. https://orcid.org/0000-0001-6399-69

3. Planalto University Center of the Federal District. Brasília, Distrito Federal, Brazil. https://orcid.org/0000-0002-8749-7536

4. Planalto University Center of the Federal District. Brasília, Distrito Federal, Brazil. https://orcid.org/0000-0002-0205-3996

5. Planalto University Center of the Federal District. Brasília, Distrito Federal, Brazil. https://orcid.org/0000-0003-1417-0871

6. Centro Universitário Planalto do Distrito Federal. Brasília, Distrito Federal, Brasil. https://orcid.org/0000-0002-8124-0262

7. Planalto University Center of the Federal District. Brasília, Distrito Federal, Brazil. https://orcid.org/0000-0001-6538-7451

8. Faculty of the Brazil Institute of Science and Technology. Anápolis, Goiás, Brazil. https://orcid.org/0000-0002-1913-1209

Received: 12/07/2021
Accepted: 17/09/2021

RESUMO

Objetivo: descrever a experiência de familiares/cuidadores de pessoas portadoras da doença de Alzheimer que estejam fazendo uso do canabidiol como forma de tratamento por intermédio do Instituto Acalme (Associação Canabis Luz Medicinal). **Método:** Trata-se de uma pesquisa qualitativa de método descritivo por meio de entrevista com o familiar ou cuidador de pessoa com a doença, que estejam em tratamento há mais de 6 meses. **Resultados:** Diante dos dados coletados, foi possível detectar que o uso do canabidiol como terapêutica ainda não é muito esclarecido, fazendo com que o tratamento se torne de difícil acesso em vários aspectos. **Conclusão:** Para a saúde esse estudo é relevante para que se possa entender um pouco mais sobre o tema visto que é uma terapêutica que vem crescendo a cada ano.
Descritores: Alzheimer; Tratamento; Canabidiol.

ABSTRACT

Objective: to describe the experience of family members/caregivers of people with Alzheimer's disease who are using cannabidiol as a form of treatment through the Acalme Institute (Association Cannabis Medicinal Light). **Method:** This is a qualitative research of descriptive method through interviews with the family member or caregiver of a person with the disease, who have been in treatment for more than 6 months. **Results:** Given the data collected, it was possible to detect that the use of cannabidiol as therapy is not yet very clear, making the treatment difficult to access in several aspects. **Conclusion:** For health this study is relevant so that one can understand a little more about the subject since it is a therapy that has been growing every year.
Descriptors: Alzheimer's; Treatment; Cannabidiol.

RESUMEN

Objetivo: describir la experiencia de familiares/cuidadores de personas con enfermedad de Alzheimer que están utilizando cannabidiol como forma de tratamiento a través del Instituto Acalme (Asociación Cannabis Medicinal Light). **Método**: Se trata de una investigación cualitativa de método descriptivo a través de entrevistas con el familiar o cuidador de una persona con la enfermedad, que llevan más de 6 meses en tratamiento. **Resultados:** Dados los datos recogidos, fue posible detectar que el uso del cannabidiol como terapia aún no está muy claro, lo que dificulta el acceso al tratamiento en varios aspectos. **Conclusión:** Para la salud este estudio es relevante para que uno pueda entender un poco más sobre el tema ya que es una terapia que ha ido creciendo cada año.
Descriptores: Alzheimer; Tratamiento; Canabidiol.

ORIGINAL

Introduction

Alzheimer's disease is a disease that enters the paraments of incurable diseases because it is classified as neurodegenerative, due to the progress of the disease the symptoms are worsening due to the death of brain cells[1], causing a kind of dementia or loss of cognitive functions, reducing the ability to relate socially, interfering in personality, memory, orientation, which may also affect language, causing the patient to have difficulties in communicating verbally, in addition to impairing the emotional state of the individual, and may cause depressive, anxious symptoms, delusions, hallucinations and even aggressiveness.[2]

Most of the victims are the elderly population, and may present early cases, but are rarer and isolated cases due to pre-existing diseases such as Down Syndrome or people with genetic mutation.[3-4]

The advance of Alzheimer's Disease (AD) is slow, and may be more than 10 years even if the cause of the disease is not yet known, there are some brain lesions that are characteristic, and that are noticeable even before the onset of symptoms, which begin to become apparent with insidious impairments of recent memory and cognitive functions.[1,5]

Pharmacological treatment is based on relieving some symptoms caused by the disease through drugs such as "donepezila", "galantamine", "rivastigmine" and "memantine", which will provide better quality of life to the carrier of the disease by blocking enzymes that cause the symptoms. However, this method of treatment is very limited, in addition to exposing the patient to various side effects of medications in use, integrative therapies with the specific use of herbal medicines such as cannabis, has been gaining space within the treatments of some diseases being one of them AD, bringing benefits and quality of life to the patient coming out of an integrative therapy and transforming into integrated therapy.[6-7]

The therapeutic use of Cannabis in the treatment of AD has efficacy as a protective, anti-inflammatory and antioxidant neuroagent[8], delaying the progressive effect of the disease. DOSES OF CBD and/or THC decrease the concentration of a protein in the brain called beta-amyloid which is the main suspect for the onset of Alzheimer's, as this protein affects synapses and signals inflammation in the neuron to immune cells, causing deficient cells to be destroyed.[9]

Within so many studies already conducted on the benefits of cannabinoids, the use in practice as an integrative therapy, even though it is within the classifications of herbal medicines and medicinal plants, is still very limited in some countries including Brazil, which makes it even more difficult to access this form of non-pharmacological therapy for patients with AD, for this reason the ACALME institute has been creating, to provide information about cannabidiol, the law processes for authorization of use, as well as helps populations to have access to doctors who assist in the prescription, follow-up and possible processes to obtain authorization for use. How is it possible to describe the experience of family members/caregivers of people with Alzheimer's who are using canabidol?

The aim of this study was to describe the experience of family members/caregivers of people with Alzheimer's who are using Cannabidiol through the ACALME-Association Cannabis Light Medicinal Institute.

This study becomes important because the use of cannabidiol as a herbal medicine can help in the treatment of several chronic and degenerative diseases, bringing more comfort to the family and patients with the disease, avoiding the abuse of drugs, besides contributing to students and health professionals who are adept at the use of medicinal plants.

Method

The present study is part of the descriptive research line of qualitative character. Given the nature of the object, it was decided to develop a descriptive case study according to the assumptions of Robert K.Yin.

Data collection began after the authorization of the Ethics and Research Committee (CEP) whose protocol follows no. 5,069,622, then the person interested in participating filled out a questionnaire via "Forms" for analysis of participation criteria. Finally, the person should be in accordance with the Informed Consent Form (TCLE), in order to hold the meeting according to the participant's availability.

According to Resolution No. 510, of April 7, 2016 ethics is considered as a human construction that involves the historical, social, cultural, moral and religious part of each individual, as well as their habits and customs, so it is considered that ethics in research should demand the recognition of human dignity and preservation to the participants, thus demanding respect and guaranteeing the rights of those involved in the research, in order to predict and prevent possible harm to these participants, thus refusing any form of prejudice.[10]

The site used for study was in the Association Cannabis Light Medicinal – ACALME, which has a public group on the social network WhatsApp (WPP), which was created in 2019, this group is composed with patients, relatives of patients, health professionals, legal, and aims to pass information about the benefits of treatments with medicinal cannabis through scientific articles, projects, experiences and others. For the research to be carried out, permission was requested, and it only started after the cep's authorization.

The subject for this study was the family caregiver of the person with Alzheimer's who has been using medicinal cannabis through cannabidiol for more than 6 months, who was digitally invited after the cep's authorization.

The subject agreed to participate collaboratively in this research by signing the Informed Consent, and in order for the research objectives to be achieved, the subject had to meet the following criteria: being the family member or official caregiver of the alzheimer's patient; the carrier made use of conventional medications; voluntarily accepted to participate in the research; the carrier used medicinal cannabis for 6 months; signed the ETS; family members or caregivers were older than 18 years; He was a member of the acalme institution; he enjoyed good mental health, which corresponds to being well with himself and with others, knew how to deal with good emotions and unpleasant ones, but that somehow were part of life and that recognized their limits and sought help when necessary, had good cognitive function of time, space and

person, possessed verbal abilities, attention and concentration, sense of judgment and reasoning. Exclusion criteria include: a family member who was not an official caregiver of alzheimer's patients; alzheimer's person who does not use conventional medications; family member who was unwilling to tell about his experience; person who was not under follow-up for at least 6 months of cannabidiol use; under 18 years of age; and that he did not enjoy good mental health.

The research was conducted through a focal interview, where the respondent is questioned for a short period of time. The answers happen spontaneously and are taken as an informal conversation, but there is a set of questions with the aim of directing the interview.

The interview was conducted with the caregiver of a person with Alzheimer's for more than 15 years who uses cannabidiol as therapy. It was given through a virtual meeting using the video call of WhatsApp, with the help of a script to direct the interview and prevent the blur, aiming to hear from the family member about his experience with cannabidiol.

Data analysis began with transcription and organization of the reports, ensuring anonymity for the study participant, through the choice of a random name. It is important to remember that the qualitative analysis of the semi-structured interview aims to explore the different representations about the object studied. The central ideas that had the same meaning, or equivalent meaning, or complementary meaning were grouped. The next step was to name each group with a title from the report.

Results

The results of the research, the caregiver José allowed to identify three major discursive areas: life history about the diagnosis; about care and history about adoption of cannabidiol.

Life story about diagnosis

> "My mother she worked until a certain time in the bank, met my father, got married, when they got married left work to take care of the children, so she lived taking care of us, and from there she did not work anymore, my mother had 3 children, was always housewife, very active, vaidosa today she is 77 years old, her Alzheimer's must have started in her 60s."
>
> "When I realized she was forgetting a lot of things."
>
> "First of all, I was observing that at the beginning of the disease, she started leaving a lot of things open, like a faucet, a refrigerator door, a stove, she repeated the same story several times, she was very forgety, things she did the same day she forgot."
>
> "Today she remembers her children, her husband, is alone in the house, can not leave the house alone, I take her to the psychiatrist, neurologist and geriatric every 5 months."
>
> "Her Alzheimer's isn't very aggressive, it's a softer Alzheimer's."

"With regard to basic activities, she can handle combing her hair, in fact she has a habit of combing her hair and washing her hands, that's mania, every time she combs her hair and washes her hand, not to do anything, cook not the bill, take a bath not from the account, so she turns on the shower and passes the soap, but so cleaning, quality she does not account no, bath is the caregiver who gives, clothes have to put and take off. She's just combing her hair, washing her hand and brushing her teeth. Today what she does physical activity is walking and pilates 2x a week."

"This disease, what I find very difficult of her is you to accept, I took a long time to accept, to believe and today I accept quiet and with regard to cannabidiol what I noticed well, which had a very great improvement, was with regard to appetite, before she was not able to eat alone and was not eating anything, today she eats alone and eats well."

History about care

"I'm the one who takes care of her, by my calculations, she must have Alzheimer's about 15 years ago. The challenge, the hardest thing I found, because we are not used, with the disease person goes back to being a child, the hard work, you have to keep watch all day, take everything back and not put back, return to be a child literally, poop and pee in my pants, I had to put diaper for her to pee and coconut the night so she does not get dirty bed, So, back to being a child, unless the time she's sleeping, awake you have to watch her 24 hours understood? Because you can fall, you can take something, take wrong medicine, you have to hide key, you have to hide medicine, poison, why you go back to being a child and this extreme attention that I have to have, for those who are close is very stressful, it is very stressful, you have to have a lot of patience, for those who have the disease is great, she doesn't feel anything, she's in perfect condition the hard part is who takes care right, who is around, and my mother had 3 children and what cares most is me, my sisters, they take care of their way, one lives outside and another works all day as a teacher and goes there only at night, I have a quieter schedule, I'm taking care of her all day."

History on the adoption of cannabidiol

"I took a long time to take her to the doctor and start treating, she took some medications and there came a certain moment that these medications gave a stagnant in the effects, and I had already read on the internet, had acquaintances who had already taken, I was informing and I learned of the Association (ACALME), I contacted and asked for cannabidiol, because I was feeling that my mother besides being without the effects of medications, she was with very little appetite and losing too much weight. And what I felt, in one of the best effects was with regard to appetite, why she went back to eating, having an appetite and went back to eating alone. My mother was always very calm, so cannabidiol didn't work for her with regard to aggression, what I felt was that she was more willing and with more appetite."

"With regard to medications, she takes exalomped of 15 which is an adhesive, OXOSONIO, DONAREN, and these medications are very good, but there comes a certain point of the disease that they give a stagnant and I felt a very great improvement in cannabidiol."

> "No, with regard to cannabidiol, her memory remains the same, she never forgot her children or her husband."

> "I think it's 5%, I started to drop the first week, then I started giving 2 and now I give her 3 drops twice a day, because I tried the most, but I felt like she got a little grog, so I give 3 likes and feel a good effect."

Discussion

Alzheimer's disease is a pathology classified as neurodegenerative that causes a decrease in cognitive functions, reducing the ability to work and relationships. Over time and with the progress of the disease, it can also interfere with the behavior and personality of the carrier and consequently causing a loss of memory.[11]

At the beginning of the disease, the patient may remember very old events and end up forgetting things considered simpler such as having a meal or remembering what food he ingested even though he had just performed these activities.[11]

Over time and the evolution of the disease, the patient's daily life suffers a great impact, thus affecting the ability to learn, care, guidance, understanding and language, increasingly in need of help and becoming dependent even on daily and basic routines such as personal hygiene and food.[12]

Alzheimer's is the most common cause of dementia that is a group of brain disorders capable of causing the loss of intellectual and social skills. In AD brain cells degenerate to death causing a constant decrease in memory and mental function.[13]

The picture of dementia varies according to severity being classified from milder stages at the beginning of the decrease in the brain functioning of a person, to reaching a greater stage the person becomes completely dependent on other people for performing basic activities in their daily routine.[12]

Alzheimer's disease in general settles quietly and develops continuously and slowly over several years. The pathological changes in neurons and biochemistries that occur in AD can be separated into two areas: changes in structures and changes in neurotransmitters. Structural alterations include neuro fibrillar enovelados, neuritic plaques and changes in amyloid metabolism, as well as sinapotic damage and neuronal death. Changes in neurotransmitter systems are connected to structural changes that are pathological changes that happen in a disorderly manner in the body of carriers of the disease. Some neurotransmitters are significantly or relatively affected, thus indicating a pattern of aggravation in the systems.[14]

AD is not considered as a natural aging process, but rather a metal disorder that has as characteristic a brain atrophy that presents a configuration of longer cortical grooves and cerebral ventricles larger than those considered normal in an aging state, these changes are possible to be visualities through a ct scan or through magnetic resonance imaging (MRI). Macroscope examination of the brain in patients with AD points to a relevant atrophy in the frontal, temporal and parietal regions affecting mainly the cortical areas. The visualization of histopathological changes through microscopic examinations is also feasible, and neuronal alterations and sinaptic degenerations that occur intensely can be added, specifically in the pyramidal layers of the cerebral cortex region, limbic

structures and associative cortexes, with the preservation of primary cortical regions. The microscope examination is responsible for presenting the presence of failures in the senile plaques and nurofibrillary tangles, vascular ganularde degeneration, astrocotic glucose and amyloid angiopathy.[15]

The diagnosis of AD can be made in two ways, clinically or differentially. The clinical diagnosis is made through exclusion, initially occurring a screening where depression and laboratory tests are evaluated, with a focus on the results of thyroid functions and vitamin Blevels12. In patients with memory problems, the diagnosis is based on the identification of specific cognitive modifications.[16]

The criteria for AD are divided into five: probable diagnoses, probable findings that sustain the disease, findings consistent with a probable diagnosis, features that reduce the chance of probable diagnosis and possible clinical diagnosis for AD. The probable diagnosis for AD includes the presence of some dementia syndrome, deficits in 2 or more areas of cognition, progressively worsening of memory and/or other intellectual functions, initiating symptoms between 40 and 90 years of age, leading to no preexisting diseases that may cause the syndrome. Likely findings that support AD include loss or weakening in speech capacity, difficulty verbalizing due to inability to join the lips, jaw and tongue, and difficulty or inability to recognize objects progressively, impairment of daily activities and behavioral changes, family history and non-specific findings, or normal test results, electroencephalogram and cranial tomography (CT).[17]

Likely diagnosis based on consistent findings include related psychiatric and vegetative symptoms such as depression, insomnia, lack of behavioral control, delusions, hallucinations, weight loss, normal CT for the patient's age, seizures in advanced disease, other neurological imbalances such as increased muscle tone, myoclonus (rapid tremors in the body), or gait disorder. Features that reduce the chance of a diagnosis of AD are cases in which symptoms happen very quickly, convulsions, gait disorders, focal neurological findings early in the course of the disease.[18]

And finally, the possible diagnosis in a clinical way can be made based on the picture of dementia syndrome when some conditions are added, when there are no other neurological, psychiatric, or other disorders capable of causing dementia; the presence of unusual findings at the onset or in the clinical course, or when there is the presence of another disorder that may cause in a picture of dementia, but that this is probably not the only cause.[18]

For the individual to be included or not in conventional treatment, some requirements are required. For there to be an inclusion in the AD treatment protocol, it is necessary that the patient meets all the criteria: probable diagnosis, according to (NINCDS-ADRDA); who has a cognitive test score of 12 and 24 for patients with more than 4 years of schooling and 8 and 21 for patients with up to 4 years of schooling in the MSI (mini mental state examination); mild or moderate dementia evaluation scale and CT or MRI of the skull and laboratory tests that rule out the possibility of other diseases that may affect the patient's mental state such as anemia, altered sodium dosage, glucose, urea, change in TSH dosage, etc. In order to exclude the treatment protocol, it includes patients who manifest at least one of the following conditions: recognition of inability to approve treatment; uncompensated brain lesions; severe cases of heart failure or arrhythmia; hypersensitivity to medicines and severe liver or kidney failure.[17]

The treatment of AD for patients who comply with the prerequisites should be multidisciplinary, paying attention to all the various signs and symptoms caused by the disease. The use of drugs is used in most conventional treatment, with the aim of slowing the evolution of the disease and promoting greater stability in cognitive impairment, behavior and performance of daily activities, these drugs are used to control the symptoms caused by AD.[19]

The drugs that are most frequently prescribed by doctors are 'acetylcholinesterase inhibitors', which slow down the degradation of acetylcholine which is naturally secreted, providing a more significant advance. For these substances to be effective in treatment, they must cross the blood brain barrier. Drugs considered first-line for treatment are supplied in Brazil by the Unified Health System (SUS) applied by the Specialized Component of Pharmaceutical Care (CEAF) and have as main drugs for the treatment of AD Donepezil, Rivastigmine and Galantamine.[20] These drugs have pharmacological properties capable of inhibiting the degradation of the molecule acetylcholine, the neurotransmitter classically related to memory, by inhibiting the enzyme acetylcholinesterase, and for this reason are used recurrentin the initial and intermediate phase, and Memantine, which is used in the intermediate and advanced phases, assisting in the stability of patients' symptoms.[13]

In addition to the treatment of cognitive symptoms, when possible and necessary can be performed we treat for behavioral symptoms specifically depression, although treatment for patients with AD is very limited.[21]

The use of these drugs in conventional treatments is relatively high and in addition to cost, there are many side effects and interactions with other medications, where they are often intolerable for users, making it necessary to use alternative therapies for treatment that are relatively more affordable such as the use of Cannabis and its phytocannabinoids.[22]

A study was conducted in mice with induced Alzheimer's, to which they received doses of THC for a period of six weeks, with this study, it was possible to notice a significant improvement in the cognitive part, different from rats that were treated with placebos, besides presenting an improvement in short- and long-term memory, and then suggested as an effective way to treat Alzheimer's, this is because THC is a CB1 receptor agonist in the g-inhibiting protein that leads to a blockade in the release of glutamate, thus suggesting a reduction through these excitotoxicity receptors that is considered as one of the causes of neuron lesions in patients with AD.[23-24]

With regard to CBD, the studies portray a neuronal protection capacity resulting from antioxidant capacity counts o2 free radicals, which are produced in neurons from the release in high amounts of glutamate, resulting in a reduction of this form of neuronal damage favored by the deposit of β-amyloid protein.[25]

One of the difficulties in measuring the real importance of cannabis for treatments for diseases such as Alzheimer's is due to the prohibition, including clinical research on the efficacy and safety of the use of this herbal medicine, which when not censored, is so discouraged, malvista and hampered by the agencies that finance research.[26] The World Health Organization (WHO) has suggested that Cannabis be rescheduled due to evidence of its medicinal functions in specific situations. In 2014, the Federal Council of Medicine (CFM) was authorized to prescribe CBD nationwide due to the number of case reports

regarding the benefits of therapeutic use in severe pathologies. In 2015 the National Health Surveillance Agency (Anvisa) authorized the controlled use of CBD, which caused cannabidiol to fall out of the category of prohibited substances, moving to controlled substances. That same year Anvisa regulated the import of cbd, through a renewed registration annually, through the presentation of the medical report reporting the evolution of the patient, this resolution also allows institutes and associations to intermediate imports, further reducing the cost that are involved in this import process. Studies of the therapeutic properties of CBD and THC are not only related in a development of new drugs, it goes far beyond, are studies of high relevance to public health.[27]

The routine of a person diagnosed with Alzheimer's is full of challenges, requiring the presence of a caregiver constantly, especially to develop day-to-day activities such as bathing, and it is because of this dependence that the caregiver is often exhausted and on alert for 24 hours.

Final Consideration

The main objective of this study was to present the benefits of the use of cannabidiol in the treatment of people with Alzheimer's. In view of the data collected, it was possible to detect that the use of cannabidiol as therapy, and that its use is not yet very clear for the majority of the population, it becomes masked between "forbidden and sin".

The study also revealed that to obtain health and quality of life much more than medications is necessary; the family in these cases plays an important role in daily follow-up, as well as in choosing good therapy. It is the family that should provide the necessary support for the person with AD. Taking into account that the cost of the drug and access to information is still a distant one for most families in the current Brazilian reality.

Among the important choices in this type of treatment, the use of cannabidiol provides quality of life for the person with AD, making them a little more independent, with appetite, and able to perform simple activities such as combing the hair and even taking a bath alone; which is gratifying not only for those who care, but as a way to ensure autonomy for the patient.

For health, as well as for professionals in the area, the in-depth study on cannabinoids is extremely important, because the search for this form of treatment is increasing every year, being responsible for treatments of various diseases, especially neurological and neurodegenerative diseases. Thus, negative beliefs, including by professionals, can be demystified as the benefits to the patient are presented.

Finally, it is important to emphasize that studies within this context still in a discrete way need to be encouraged, because they do not receive support from government agencies or Brazilian authorities. However, the patient who chooses the use, needs to go through a long trajectory of bureaucratic processes to obtain permission for this use. Families because they are unaware of the benefits of medication, accommodate themselves or fail to seek this option also for socioeconomic reasons, because they cannot maintain treatment on a continuous basis, preventing the citizen from using constitutional rights governed as principles of the Unified Health System (SUS) that guarantee the right to life

through universality, equity and integrality of the shares. What are the real benefits of cannabidiol in the neurological part of a person with AD?

Acknowledgement

This research did not receive funding to be done.

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Correspondent Author
Yara Paiva Bittes
Planalto University Center of the Federal District
Pau Brasil Av. Lot 2. ZIP: 71916-000-Águas Claras.
Brasília, Federal District, Brazil.
ybittes15@gmail.com