Brazilian Journal of Biology®

ISSN 1519-6984 (Print)
ISSN 1678-4375 (Online)

Original Article

Cannabis oil in treating Parkinson's disease: improvement of motor and non-motor symptoms: a case report

Óleo de *Cannabis* no tratamento da doença de Parkinson: melhora de sintomas motores e não motores: relato de caso

C. T. M. I. Issa[a*], R. D. Castro[a] and K. L. G. D. Albuquerque[a]

[a]Universidade Federal da Paraíba, João Pessoa, PB, Brasil

Abstract

Parkinson's disease (PD) is characterized by progressive loss of dopaminergic neurons in the substantia nigra pars compacta, which leads to a reduction in the production of dopamine. Medication with levodopa becomes less effective as the disease progresses. Despite the excellent results observed in clinical practice with the medicinal use of Cannabis in the treatment of PD, the level of scientific evidence is still limited due to the small number of studies published in this field. We present the case of a 77-year-old man diagnosed 22 years ago with PD in an advanced stage, with significant bradykinesia, tremor, and rigidity along with the inability to maintain an upright position and walk, exacerbated by a femur fracture. He also had advanced dysphagia, resulting in a gastrostomy. Although lucid, he showed no interest in conversation and tended to become depressed and isolated. He used Prolopa® with no satisfactory therapeutic response. After starting treatment with Cannabis sativa oil, he is now able to walk around the house frequently and eat pasty food regularly without choking or broncho-aspiration episodes. There has also been a significant improvement in non-motor symptoms; he is more active, cheerful, communicative, and attentive to his surroundings. Further studies are needed to elucidate these results and the mechanisms of action of cannabinoids through which they exert possible neuroprotective and neuroreparative effects. These compelling results suggest that cannabis oil may offer a valuable and effective therapeutic option for individuals with Parkinson's disease.

Keywords: case report, Parkinson, Cannabis, cannabinoids.

Resumo

A doença de Parkinson é caracterizada pela perda progressiva de neurônios dopaminérgicos na parte compacta da substância negra, resultando na diminuição da produção de dopamina. O tratamento medicamentoso realizado com levodopa, torna-se menos eficaz com a progressão da doença. Apesar dos excelentes resultados encontrados na prática clínica com o uso medicinal da *Cannabis* para tratar a doença de Parkinson, o nível de evidência científica ainda é considerado limitado, em função do pequeno número de trabalhos publicados nessa área. Apresentamos o caso de um homem com 77 anos de idade e diagnóstico de Doença de Parkinson há 22 anos, em estágio avançado, que apresentava bradicinesia, tremor e rigidez importantes, perda da capacidade de manter-se em posição ortostática e de deambular. Essa condição foi potencializada por uma fratura de fêmur. Além de disfagia avançada, que resultou na realização de gastrostomia. Apesar de lúcido, não tinha interesse em conversar, tendendo ao desânimo e isolamento. Em uso de Prolopa®, sem resposta terapêutica satisfatória. Após o início do tratamento com o óleo de *Cannabis*, caminha dentro de casa com frequência e faz ingestão rotineira de alimentos pastosos, sem episódios de engasgo e/ou broncoaspiração. Também apresentou melhora não motora importante, está mais ativo, alegre, comunicativo e atento ao que acontece em seu entorno. Mais estudos são necessários para elucidar esses resultados e os mecanismos de ação dos canabinoides por meio dos quais eles exercem possíveis efeitos neuroprotetores e neuroreparadores. Esses resultados convincentes sugerem que o óleo de cannabis pode oferecer uma opção terapêutica valiosa e eficaz para indivíduos com doença de Parkinson.

Palavras-chave: relato de caso, Parkinson, *Cannabis*, canabinoides.

*e-mail: chahiraissa@hotmail.com; ctmiissa@gmail.com
Received: September 14, 2024 – Accepted: October 22, 2024

1. Introduction

Parkinson's disease (PD) is the second most prevalent neurodegenerative disorder, with a worldwide prevalence of 6 million people. An increase of 2.5 times is estimated over the next 30 years. Consists of neural inclusions in the form of Lewy bodies and Lewy neurites, characterized by progressive loss of dopaminergic neurons in the substantia nigra pars compacta (Palermo and Ceravolo, 2019), which results in reduced dopamine production (Tolosa et al., 2021).

The diagnosis of PD is clinical and includes cardinal motor features (e.g., bradykinesia, rigidity, resting tremor, and postural instability) and non-motor features (e.g., cognitive, behavioral, sleep, and autonomic dysfunction), which are usually progressive and may not respond to dopaminergic therapy (Santos-Garcia and de la Fuente-Fernandez, 2013), profoundly affecting the quality of life. Pharmacological treatment is with levodopa, and despite an initial significant response regarding motor symptoms, these effects become less evident as the disease progresses and medication requirements increase. Therefore, it is relevant to find therapeutic alternatives that satisfactorily control PD-related symptoms (Chaudhuri et al., 2018).

Despite the limited number of published studies regarding the effects of Cannabis in PD, in a systematic review and meta-analysis, potential benefits were identified related to the relief of tremor, anxiety, pain, improvement of sleep quality and general quality of life in these patients (Urbi et al., 2022). Given the scarcity of studies and the undeniable benefits of using cannabis oil in PD, case reports that demonstrate clinical improvements in these patients are necessary.

Considering Parkinson's disease a neurodegenerative process, in this report we present a unique case where, in addition to slowing the progression of the disease, there was recovery of motor and cognitive functions in a patient with advanced stage Parkinson's disease, after starting treatment with full-spectrum cannabis oil. Results not usually observed in clinical practice with treatments traditionally used for this clinical condition.

2. Methods

The patient's responsible family member provided informed consent for the case to be reported. The present study was approved by the Federal University of Paraíba, Brazil ethical committee, with approval number CAAE:73876223.4.0000.5188.

We present the case of a 77-year-old man diagnosed with PD 22 years ago, in 2001, currently in an advanced stage and without other chronic diseases. In 2004, according to a clinical evaluation by a neurologist, the patient showed significant bradykinesia, tremor, and rigidity, with difficulty walking and a reserved prognosis.

At medical evaluation, carried out in person by family members in March 2023, reports from healthcare professionals, such as neurologists, rheumatologists, and speech therapists, as well as examination results obtained during the disease were brought. Due to limited mobility, the patient evaluation was conducted using a video call. During the session, he remained alert but had difficulty speaking; his voice was barely audible, and he spoke sparingly. In addition, he showed minimal engagement in conversation and signs of apathy. Notable observations included a pale complexion and significant contractures in his hands and feet. According to family and caregiver reports, the patient ceased oral intake, lost the ability to stand, and communicated very little with a weak voice. Despite being lucid, he showed no interest in social interaction and exhibited tendencies toward despondency and isolation. He often appeared distant and maintained a blank stare for long periods.

The disease progresses over time, leading to loss of the ability to maintain an upright position and walk. This condition was aggravated by a femur fracture sustained in a fall three years ago. Two years ago, he developed advanced dysphagia requiring the insertion of a gastrostomy tube (GTT), a procedure that was performed six months ago (Figure 1).

In 2004, a cranial magnetic resonance imaging (MRI) scan was performed, showing a brain within normal parameters for the patient's age. One year ago, an awake electroencephalogram (EEG) was performed, showing

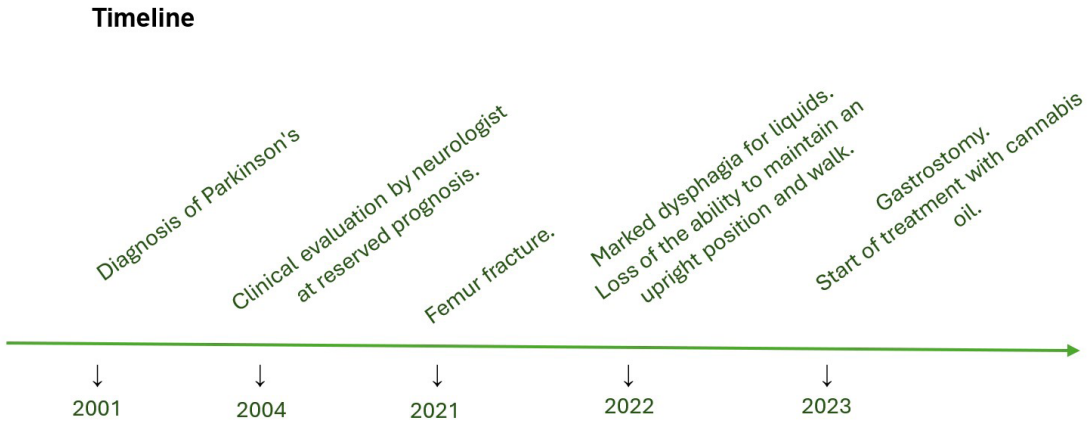

Figure 1. Historical and current information from this episode of care.

isolated slow components of high electrical amplitude involving frontopolar areas without any structural changes in the brain parenchyma.

Recent laboratory tests revealed normal serum urea, creatinine, and sodium levels, an elevated C-reactive protein level, and a urinary tract infection that has been treated. The blood count showed mild anisocytosis, white blood cells with preserved morphology with values near the upper limit, and a platelet count that appeared normal under the microscope.

He has been using Prolopa® (levodopa hydrochloride/benserazide) for many years without a satisfactory therapeutic response.

Treatment with cannabis oil was initiated on the same day as the consultation. The oil was extracted with alcohol at room temperature and is full-spectrum CBD-rich oil containing THC and other phytocannabinoids, with a concentration of 20 mg/ml de CBD. This oil was obtained from the Associação Brasileira de Apoio Cannabis Esperança (ABRACE), a private, nonprofit organization based in João Pessoa, Paraíba, Brazil.

3. Follow-up and Outcomes

On the first day of the consultation, the patient received one drop orally twice a day. On the second day, the dosage was increased to two drops twice daily, and on the third day, it was further increased to three drops twice daily. After ten days, the dosage was increased to four drops twice daily. After one month on this dosage, another adjustment was made, increasing the dosage to 5 drops twice daily (Figure 2).

After one week of treatment, the patient was able to stand up with the help of the physiotherapist and the nurse. On the 11th day of treatment, he was able to take a few steps, walking with arm support for a distance of about 2 meters. According to the nurse, he also showed a significant non-motor improvement, becoming more active, cheerful, and attentive to his surroundings. One month after starting cannabis oil, he was even more active, and the physiotherapist noticed an increase in muscle strength and improvement in communication. On the 40th day of treatment, the caregiver sent a video showing the patient walking across the entire living room of the apartment where he lives, a spacious area, still with bilateral support but with much steadier steps. On the 46th day, he was able to cross his legs on his own, and the caregiver sent a video in which the patient was able to consume pasty foods orally (yogurt and milk curd) without choking. Two months after starting cannabis oil, the patient is even more active, cheerful, and communicative. The physiotherapist reports a significant increase in muscle strength and notes that he frequently walks around the house. After routine intake of pasty foods without choking episodes, as confirmed by the nutritionist, the speech therapist has requested a videofluoroscopic swallowing study to assess the possibility of resuming oral feeding. The clinical course over time is detailed in Figure 3. According to the neurologist in charge of the case, the patient has shown significant improvement, allowing a reduction in the dosage of Prolopa® without compromising his clinical condition.

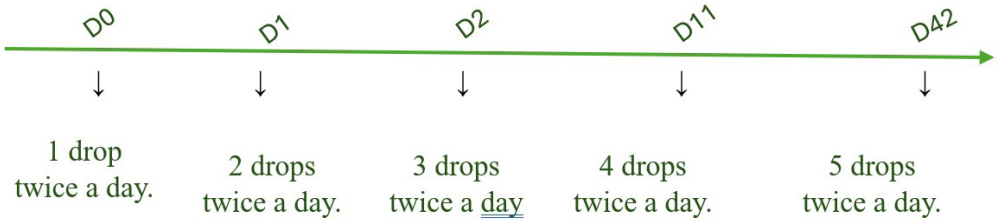

Figure 2. Protocol for adjusting the dose of Cannabis oil over time, administered to patients with Parkinson's disease.

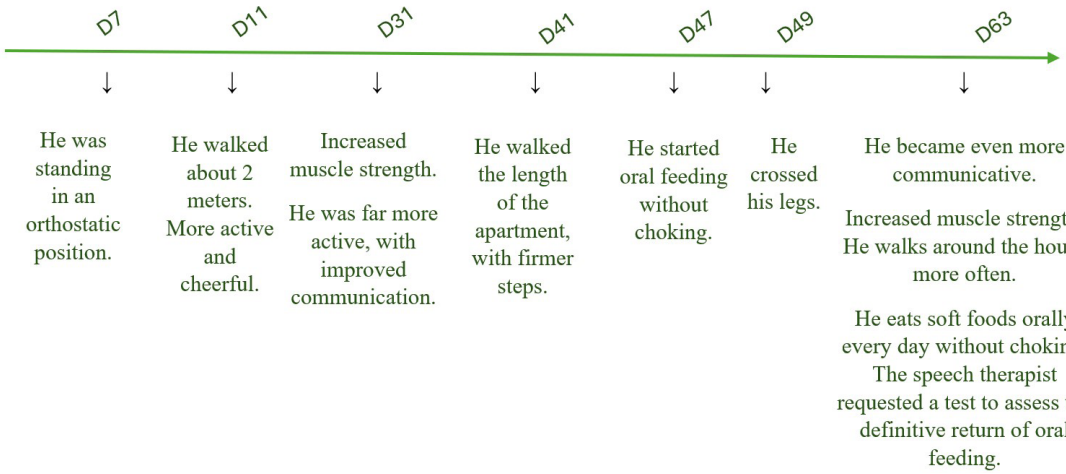

Figure 3. Clinical improvement over time in the patient with Parkinson's disease treated with Cannabis sativa oil.

4. Discussion

It is known that neuroinflammation and genetic mutations are involved in the pathogenesis of PD, leading to the destruction of dopaminergic neurons in the nigrostriatal pathway, which includes the basal ganglia (GB) – structures that regulate movements (Morano et al., 2020). The intracellular accumulation of Lewy bodies and protein inclusions forms neurites, also responsible for motor symptoms in PD (Tolosa et al., 2021).

The endocannabinoid system (ECS) has been investigated as a drug target for PD. Overexpression of ECS receptors has shown neuroprotection and reduced neuroinflammation in neurodegenerative diseases. Neuroprotective effect of ECS was demonstrated in parkisonism induced by neurotoxins through the coexpression of CB1R and GPR55. Like endocannabinoid neurotransmitters, phytocannabinoids act as ligands for ECS receptors. Delta-9-tetrahydrocannabinol (Δ9-THC) and cannabidiol (CBD) from the Cannabis plant have shown neuroprotection in animal models of PD (Cooray et al., 2020). Studies using cell cultures (Carroll et al., 2012) and primate models (van Vliet et al., 2008) have demonstrated beneficial effects in controlling motor and non-motor symptoms of PD.

CBD promotes neuromodulation, possibly due to its activity on multiple molecular targets, including the serotonin 5-HT1A receptor, as well as adenosine A2A, CB1, TRPV-1 and GPR55 receptors, abundantly expressed in the basal ganglia, the main structures involved in motor control (Morano et al., 2020).

This case reports a significant improvement in both motor and non-motor functions in a patient with advanced PD following the administration a full-spectrum CBD-rich oil containing THC and other phytocannabinoids was used (Table 1). Consistent with our findings, a study using monkey models of PD treated with Δ9-THC observed recovery of locomotor activity almost to pre-disease levels. In addition, hand-eye coordination performance was significantly improved (van Vliet et al., 2008).

As part of its modulating effect on the ECS, CBD inhibits both fatty acid hydrolase (FAAH), the enzyme that metabolizes anandamide in inactive compounds such as anandamide reuptake, increasing the levels of this neurotransmitter that produces analgesic, anxiolytic and antidepressant effects by signaling the CB1 receptor in the brain. Because the CB1 receiver is predominantly found in motor, limbic, associative, cognitive, sensory and autonomic structures (Mock et al., 2023), improvement in non -motor symptoms reported in this clinical case, such as attention, perception, communication and mood, can also be attributed to the effects of treatment with full-spectrum cannabis oil.

Reflecting on clinical practice the studies cited and corroborating the results obtained in the case reported in this study, researchers described a clinical case of an 85-year-old patient with Lewy body dementia and worsening refractory aggression to antipsychotic treatment. The patient's behavior improved rapidly after initiating treatment with a THC-rich tincture (Ramm et al., 2023).

Similar results were obtained in another case. A 71-year-old woman diagnosed six years ago with progressive gait disturbance, parkinsonism, and severe speech impairment was treated with a full extract cannabis oil with approximate proportions of the major cannabinoids of 0.5% CBD, 2% THC, 10% CBDA (cannabidiolic acid), and 7% THCA (tetrahydrocannabinolic acid). After five weeks of cannabis oil administration, her speech improved significantly. She also showed improvement in her hand tremors and regained the ability to move her limbs (Hounie and Vasques, 2019).

The improvement in coordinated swallowing function and the resumption of oral feeding in this case is likely the result of the combination of the neuroprotective and neurorepair effects of CBD (Cooray et al., 2020) combined with the orexigenic effect observed with stimulation of the CB1 receptor, like THC, observed with exogenous administration of anandamide (Mock et al., 2023).

Neurodegeneration in PD has been halted by no drug to date. Current treatments focus mainly on managing symptoms, and there are no therapies available in clinical practice to prevent neurodegeneration or repair neurons (Cooray et al., 2020). In a study using PC12 cells that had been treated with a neurotoxin, the results showed that CBD had a neuroprotective effect and suggested that CBD could help treat PD (Santos et al., 2015). The polypharmacological properties of cannabis-derived products offer distinct advantages over the current single-target pharmaceutical model and can optimize neurological treatment and serve as an effective and safe therapeutic option (Morano et al., 2020).

5. Conclusion

Although clinical cases (Ramm et al., 2023; Hounie and Vasques, 2019), animal models (van Vliet et al.,

Table 1. Clinical improvements, classified as motor and non-motor, in patients with Parkinson's disease treated with *Cannabis* oil.

Improvement of motor symptoms	Improvement of non-motor symptoms
Decreased muscle and joint stiffness.	Increased cognitive activity.
Increased muscle strength.	Happier mood.
Improved balance.	Increased focus and attention.
Resumption of walking.	Increased ability to communicate.
Greater coordination during swallowing.	Increased interest in surroundings.
Resumption of oral feeding.	Increased appetite.

2008), and cellular studies (Carroll et al., 2012) have demonstrated neuroprotective effects, beneficial in delaying neurodegeneration, the precise molecular mechanisms are not well understood. Therefore, further studies are needed to clarify these mechanisms and to understand the subsequent slowing of neurodegeneration and the neuronal repair (Cooray et al., 2020).

In this scenario, considering the scarcity of clinical studies and the undeniable benefits of using cannabis oil in Parkinson's Disease, the results presented in this clinical case highlight the notable improvement in the motor and non-motor symptoms of a 77-year-old man, in an advanced stage of the disease, in order to motivate the performance of randomized controlled clinical trials and provides the basis to make them a validated and recommended therapeutic option.

Acknowledgements

The authors are grateful to the patient and his family members who allowed their data to be used to write this article and ABRACE for providing the product for the study.

Disclosure

No conflicts of interest concerning the publication of this article.

References

CARROLL, C.B., ZEISSLER, M.L., HANEMANN, C.O. and ZAJICEK, J.P., 2012. Δ^9-tetrahydrocannabinol (Δ^9-THC) exerts a direct neuroprotective effect in a human cell culture model of Parkinson's disease. *Neuropathology Applied Neurobiology*, vol. 38, no. 6, pp. 535-547. http://doi.org/10.1111/j.1365-2990.2011.01248.x.

CHAUDHURI, K.R., POEWE, W. and BROOKS, D., 2018. Motor and nonmotor complications of Levodopa: phenomenology, risk factors, and imaging features. *Movement Disorders*, vol. 33, no. 6, pp. 909-919. http://doi.org/10.1002/mds.27386. PMid:30134055.

COORAY, R., GUPTA, V. and SUPHIOGLU, C., 2020. Current aspects of the endocannabinoid system and targeted THC and CBD phytocannabinoids as potential therapeutics for Parkinson's and Alzheimer's diseases: a review. *Molecular Neurobiology*, vol. 57, no. 11, pp. 4878-4890. http://doi.org/10.1007/s12035-020-02054-6. PMid:32813239.

HOUNIE, A.G. and VASQUES, M.A.A., 2019. Neurological improvement with medical cannabis in a progressive supranuclear palsy patient: a case report. *Medical Cannabis and Cannabinoids*, vol. 2, no. 2, pp. 65-68. http://doi.org/10.1159/000503864. PMid:34676336.

MOCK, E.D., GAGESTEIN, B. and VAN DER STELT, M., 2023. Anandamide and other N-acylethanolamines: A class of signaling lipids with therapeutic opportunities. *Progress in Lipid Research*, vol. 89, pp. 101194. http://doi.org/10.1016/j.plipres.2022.101194. PMid:36150527.

MORANO, A., FANELLA, M., ALBINI, M., CIFELLI, P., PALMA, E., GIALLONARDO, A.T. and BONAVENTURA, C.D., 2020. Cannabinoids in the treatment of epilepsy: current status and future prospects. *Neuropsychiatric Disease and Treatment*, vol. 7, no. 16, pp. 381-396. http://doi.org/10.2147/NDT.S203782. PMid:32103958.

PALERMO, G. and CERAVOLO, R., 2019. Molecular imaging of the dopamine transporter. *Cells*, vol. 8, no. 8, pp. 872. http://doi.org/10.3390/cells8080872. PMid:31405186.

RAMM, R.M., LERNER, Z.I., LEVY-MEEKS, G.S., BURKE, R.V., RAVEN, M.C., SONG, A. and GLASS, M.H., 2023. A case report of treatment-resistant agitation in dementia with lewy bodies: medical marijuana as an alternative to antipsychotics. *Journal of Palliative Medicine*, vol. 26, no. 5, pp. 737-740. http://doi.org/10.1089/jpm.2022.0343. PMid:36576970.

SANTOS, N.A.G., MARTINS, N.M., SISTI, F.M., FERNANDES, L.S., FERREIRA, R.S., QUEIROZ, R.H.C. and SANTOS, A.C. 2015. The neuroprotection of cannabidiol against MPP+-induced toxicity in PC12 cells involves trkA receptors, upregulation of axonal and synaptic proteins, neuritogenesis, and might be relevant to Parkinson's disease. *Toxicology in Vitro*, vol. 30, no. 1(Pt B), pp. 231-240. http://doi.org/10.1016/j.tiv.2015.11.004.

SANTOS-GARCÍA, D. and DE LA FUENTE-FERNANDEZ, R., 2013. Impact of non-motor symptoms on health-related and perceived quality of life in Parkinson's disease. *Journal of the Neurological Sciences*, vol. 332, no. 1-2, pp. 136-140. http://doi.org/10.1016/j.jns.2013.07.005. PMid:23890935.

TOLOSA, E., GARRIDO, A., SONJA, W.S. and POEWE, W., 2021. Challenges in the diagnosis of Parkinson's disease. *Lancet Neurology*, vol. 20, no. 5, pp. 385-397. http://doi.org/10.1016/S1474-4422(21)00030-2. PMid:33894193.

URBI, B., CORBETT, J., HUGHES, I., OWUSU, M., THORNING, S., BROADLEY, S., SABET, A. and HESHMAT, S., 2022. Effects of Cannabis in Parkinson's disease: a systematic review and meta-analysis. *Journal of Parkinson's Disorders*, vol. 12, no. 2, pp. 495-508. http://doi.org/10.3233/JPD-212923. PMid:34958046.

VAN VLIET, S.A.M., VANWERSCH, R.A.P., JONGSMA, M.J., OLIVIER, B. and PHILIPPENS, I.H.C.H.M., 2008. Therapeutic effects of Delta9-THC and modafinil in a marmoset Parkinson model. *European Neuropsychopharmacology*, vol. 18, no. 5, pp. 383-389. http://doi.org/10.1016/j.euroneuro.2007.11.003. PMid:18222654.