Marijuana for Parkinson's Disease?

by **DIKSHA MOHANTY, MD, and STEVEN LIPPMANN, MD**
Dr. Mohanty is Research Scholar and Dr. Lippmann is Emeritus Professor at the University of Louisville School of Medicine in Louisville, Kentucky.

Innov Clin Neurosci. 2019;16(1–2):33–34

This ongoing column explores off-label or emerging treatment options, drug development trends, and theoretical concepts in the field of neuroscience.

ABSTRACT

Marijuana is popular in the United States and is being widely legalized for recreational and medicinal purposes. It remains a Schedule 1 substance without fully proven risks and benefits; yet, it is increasingly available in many US states and territories. Cannabis might have medicinal efficacy in Parkinson's disease as a form of medical marijuana. Endocannabinoid receptors exist throughout the nervous system and are documented to influence receptors affecting a wide variety of areas. Neuroprotective aspects might be induced by cannabis exposure that might yield benefit against the nigrostriatal degeneration of patients with Parkinson's disease. Animal investigations support suggestions of improvement in bradykinesia and/or tremors, but this is unsubstantiated in human studies. However, some patient surveys and anecdotal or case reports indicate that marijuana attenuates some motor manifestations of parkinsonism and also of non-motor, mood and/or cognitive symptoms. Medical marijuana might benefit motor and nonmotor aspects of Parkinson's disease patients. Currently, these assertions are not substantiated in human investigations and cannabis can also induce side effects. Until studies clarify the safety and efficacy of pharmacotherapy with cannabis products, medical marijuana remains largely without scientific endorsement. Research has yet to document the full benefits, risks, and clinical applications of marijuana as a treatment for patients with Parkinson's disease.

KEYWORDS: cannabis, marijuana, medical marijuana, neurology, Parkinson's disease, parkinsonism, motor symptoms, stiffness, rigidity, bradykinesia, tremor

Cannabis is becoming increasingly popular in the United States.[1] Many states have approved recreational marijuana, and several others allow medical and/or additional usages.[1] Medical marijuana is prescribed for a variety of indications; now, it even has possible application for people with Parkinson's disease (PD). Cannabis might provide relief at diminishing bradykinesia, stiffness, rigidity, and tremors.

LEGALITY

Marijuana is a Schedule 1 substance, and without definitive proof of efficacy and/or safety, it is not nationally approved for medical indications. However, pharmaceutical marijuana is legal in 29 states, Puerto Rico, Guam, and the District of Columbia.[1] Variations exist within the laws of these states/territories, with some states imposing restrictions on tetrahydrocannabinol (THC) content, while permitting higher concentration cannabidiol (CBD) products. Seventeen states have low-THC, high-CBD laws in effect.[1]

MARIJUANA

There are two species of cannabis—sativa and indica—and many types of cannabinoids have been identified. Sativa strains have high quantities of THC, which can produce euphoria, while indica contains more CBD.[2] Both cross the blood brain barrier and can exert neurotropic effects. THC is more psychoactive and is the recreational component of marijuana. Cannabidiol, being less psychoactive, is commonly employed as an analgesic, sedative, anti-emetic, and/or as an appetite stimulant.[2,3]

NEUROBIOLOGY

Endocannabinoid receptors exist in the brain, particularly at the cortex, cerebellum, basal ganglia, hippocampus, spinal cord, and peripheral nerves.[4] These receptors control muscular movements and appear to confer anti-epileptic, sedative, anxiolytic, anti-psychotic, anti-oxidant, and neuroprotective properties. These receptors might also exhibit anti-emetic, antineoplastic, antidiabetic, anti-inflammatory, and anti-ischemic effects.[5] Cannabidiol binds to cannabinoid-1 (CB1) receptors in the central nervous system (CNS), while CB2 receptors have more influence on the immune system.[6]

MECHANISM

Animal research substantiates evidence of anti-oxidant action by THC and CBD, which might provide neuroprotection against

FUNDING: No funding was provided.
DISCLOSURES: The authors have no conflicts of interest relevant to the content of this article.
CORRESPONDENCE: Steven Lippmann, MD; Email: steven.lippmann@louisville.edu

progressive degeneration of nigrostriatal dopaminergic neurons in patients with PD.[7] CB receptors upregulate in response to noxious stimuli to mitigate inflammatory damage. In animals, CB1 antagonists lowered bradykinesia, while CB1 agonists reduced tremor; however, these benefits have not been demonstrated in patients who exhibit PD signs and symptoms.[8] However, patient surveys report alleviation of non-motor symptoms, specifically depressed mood, fatigue, and memory impairments.[9] Additionally, there are anecdotal accounts of neurological efficacy at decreasing parkinsonian motor manifestations.

PHARMACOTHERAPY

Optimum dosing that achieves efficacy while minimizing adverse effects remains to be established. Current information might not be generalizable to the individual need of each patient. Single case reports support cannabis as a therapeutic agent.[10] Topical and oral cannabinoids are optimally provided in solvents due to their lipophilic nature. Starting at low dosages in cannabis-naïve individuals and utilizing slow increases in dosage help minimize adverse consequences. Clinical efficacy in patients with PD is directed toward bradykinesia, stiffness, rigidity, and tremors, which is mediated by nigrostriatal neurons.[10]

ADVERSITIES

Side effects vary in accordance to THC and CBD formulations, and they include fatigue, dizziness, nausea, xerostomia, anxiety, headache, visual changes, impaired cognition, cough, and/or palpitations.[10] Driving and operating potentially dangerous equipment is not recommended for 8 to 12 hours after ingestion. Cannabis products are contraindicated during pregnancy or lactation and for people with cardiac decompensation.[10] Marijuana is ill-advised for children or young adults until the brain is fully developed.[11] Smoking cannabis has its own inherent risks. Beyond neurodevelopmental concerns, cannabis also has unclear risk for cardiac dysfunction and psychiatric concerns, such as for the emergence of depression and/or psychosis.

CONCLUSION

Marijuana has been shown to attenuate motor and nonmotor signs and symptoms of PD. However, there are limitations to the available research, including small sample sizes and lack of standardized clinical outcome measures. Neurologic manifestations of PD might be alleviated with cannabis products, but such assertions are yet be established in reference to patient-specific factors, such as disease stage, target symptoms, and prior levodopa exposure, and dosages of cannabis product have yet to be established. Further research will reveal the efficacy and safety of medical marijuana for patients with motor manifestations of parkinsonism. Until then, pharmacotherapy with cannabis should be considered and applied with caution.

REFERENCES

1. State Medical Marijuana Laws. http://www.ncsl.org/research/health/state-medical-marijuana-laws.aspx. Accessed June 11, 2018.
2. Kluger B, Triolo P, Jones W, Jankovic J. The therapeutic potential of cannabinoids for movement disorders. *Movement Dis*. 2015;30(3):313–327
3. Marijuana dosing, indications, interactions, adverse effects, and more. https://reference.medscape.com/drug/cannabis-ganja-marijuana-343687. Accessed June 11, 2018.
4. Oberbarnscheidt T, Miller N. Pharmacology of marijuana. *J Addict Res & Ther*. 2017;S11:012.
5. Zuardi A. Cannabidiol: from an inactive cannabinoid to a drug with wide spectrum of action. *Revista Brasileira de Psiquiatria*. 2008;30(3):271–280.
6. Venderova K, Ruzicka E, Vorisek V, Visnovsky P. Survey on cannabis use in Parkinson's disease: subjective improvement of motor symptoms. *Movement Dis*. 2004;19(9):1102–1106.
7. García-Arencibia M, González S, de Lago E, et al. Evaluation of the neuroprotective effect of cannabinoids in a rat model of Parkinson's disease: importance of antioxidant and cannabinoid receptor-independent properties. *Brain Res*. 2007;1134:162–170.
8. Fernández-Ruiz J, Moreno-Martet M, Rodríguez-Cueto C, et al. Prospects for cannabinoid therapies in basal ganglia disorders. *Br J Pharm*. 2011;163(7):1365–1378.
9. Kindred J, Li K, Ketelhut N, et al. Cannabis use in people with Parkinson's disease and multiple sclerosis: a web-based investigation. *Comp Ther in Med*. 2017;33:99–104.
10. MacCallum C, Russo E. Practical considerations in medical cannabis administration and dosing. *Eur J Int Med*. 2018;49:12–19.
11. Naik S, Kolikonda M, Prabu A, et al. Marijuana on the brain—a concern. Innov Clin Neur. 2018;15(1–2):12.

ICNS