

Medical cannabis as an alternative therapeutics for Parkinsons' disease: Systematic review

Source: <https://pubmed.ncbi.nlm.nih.gov/32351233/>

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Abstract

Objectives

1) to evaluate the efficacy of medical cannabinoids (MC) by appraising the quality of evidence from clinical studies 2) to explore the factors hampering the MC use in clinical practice of Parkinson's disease (PD).

Methods

We performed a systematic review through various databases. The quality of 14 studies was assessed by Cochrane risk bias (5 randomized controlled trials- RCT) and Newcastle-Ottawa scale (9 uncontrolled studies).

Results

The positive effects on motor (5 studies) and non-motor symptoms (4 studies) described in uncontrolled studies have not been confirmed by the few and small RCTs. Only one RCT found a reduction of levodopa-induced dyskinesias, another a reduction in anxiety and tremor amplitude in an anxiogenic situation, while the remaining three without effect on motor/non-motor symptoms. Physical and psychological symptoms are among the most common side effects.

Conclusions

There is insufficient evidence to reform international legislation regarding cannabis use in PD practice.

Introduction

Parkinson's disease (PD) is a progressive neurodegenerative disease affecting 4.5 million worldwide with high lifetime cost and disability [1]. Currently, there are no disease-modifying drugs available for PD while levodopa and other standard symptomatic treatments provide some limited relief but come with side effects, such as response oscillations and levodopa-induced dyskinesia (LID), in some cases just after 24 months of levodopa exposure. Moreover, antiparkinsonian medicine is responsible for a worldwide range of 22.00–58.00% of direct costs for patients with PD [1]. Therefore there is a pressing need for alternative efficacious treatment strategies with fewer adverse effects and healthcare costs.

Cannabis based products for medicinal use, containing cannabinoids derived from the Cannabis sativa plant, including Δ^9 -tetrahydrocannabinol (THC), and cannabidiol (CBD), are one such interesting class of agents with potential efficacy in various diseases, including cancer, glaucoma, and multiple sclerosis. Several lines of evidence demonstrate that the striatal endocannabinoid system undergoes a dramatic rearrangement after dopamine depletion, both in rodent and primate models of PD, as well as in PD patients. Indeed, a close interplay between the endocannabinoid and dopaminergic system exists, both in the modulation of synaptic function and regulation of motor behavior, through specific G protein-coupled cannabinoid receptors (CB1 and CB2) in the basal ganglia [2]. As an example, CB1 knockout mice exert lower locomotor activity. So far, despite an increased knowledge of CBs–DA interactions at the molecular level, the clinical relevance of CB-based therapies on PD motor symptoms has not been systematically evaluated.

Given the expanding request of the patients, clinical and preclinical studies are urgently needed to investigate the physiological and neurological effects of cannabis use in PD. Previous reviews focused

on experimental and clinical data about the therapeutic potential of cannabinoids in PD [3,4]. The aim of this systematic review is twofold: 1) to provide a more in-depth evaluation of the efficacy of medical cannabinoids (MC) by appraising the quality of evidence from clinical studies 2) to explore the factors hampering the use of MC in clinical practice.

Section snippets

Literature search strategy

We performed a systematic review, based on the PRISMA guidelines (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) [5] (Fig. 1). The MEDLINE database was used to seek related publications in the literature from 1970 to October 2019: “cannabinoids” or “cannabis” or “tetrahydrocannabinol” or “THC” or “cannabidiol” AND “Parkinson's disease” (MeSH Terms). The process of literature retrieval consisted of three steps: (1) retrieve associated systematic reviews and

Results of the database

From a total of 228 identified articles, 114 were excluded as duplicates, 27 were excluded after title and abstract screening because they were not related to the subject (Fig. 1). 88 articles remained for full-text review. No further relevant citations were found from weekly electronic database updates up to November 1, 2019. Finally, 14 of the 87 studies were included in this systematic review (total 866 participants).

We could not perform a meta-analysis due to the high variability of

Conclusions

Despite the increasing use of cannabis for PD, there is a lack of consensus regarding the efficacy and scope of adverse effects of the drug, and this is reflected in the diverse recommendations for its use across different countries. Collectively, current data suggest that there is insufficient evidence to recommend the use of cannabis for the motor symptoms in PD, while its safety still remains unclear. Currently, until further controlled studies are performed, and until the long-term results

Patient consent

Not required.

Grant support

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

CRedit authorship contribution statement

Anastasia Bougea: Conceptualization, Methodology, Software, Data curation, Writing - original draft, Visualization, Investigation, Writing - review & editing. Christos Koros: Conceptualization, Methodology, Software, Data curation, Writing - original draft, Visualization, Investigation, Writing - review & editing. Athina-Maria Simitsi: Data curation, Writing - original draft, Visualization, Investigation, Writing - review & editing. Chrysa Chrysovitsanou: Visualization, Investigation, Writing -

Declaration of competing interest

None.

Acknowledgements

none.

Research data for this article

Data not available / Data will be made available on request

Further information on research data

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