Physician-Guided Medical Cannabis Treatment for Comorbid Anxiety and Depression Disorders in a Canadian Multidisciplinary Clinic: A Retrospective Review

ABSTRACT

Objective

Glioblastoma multiforme (GBM), also called grade IV astrocytoma, is an aggressive, malignant brain tumor with a low treatment success rate, particularly in patients with immune checkpoint-active tumors. These types of tumors are associated with a 5-year survival rate of <3%. Targeted treatments specifically designed for GBM are urgently needed. The aim of this study was to evaluate the effects of chemovar-specific cannabis extractions (CSCEs) in patients with GBM using liquid chromatography-mass spectrometry (LC-MS).

Method

The CSCEs were obtained with polar solvents and analyzed using LC-MS in patients with GBM. The complex nature of cannabis compounds has hindered the personalization of standard cannabis medicines for GBM due to the unknown synergistic effects of multiple compounds. To address this challenge, the present study focused on exposing U570 brain tumor cells to chemovar fractions extracted using polar (upper layer) and nonpolar (lower layer) solvents.

Result

Our approach permitted the isolation of a broader spectrum of constituents present in the cannabis extract. Using LC-MS in conjunction with nuclear magnetic resonance spectroscopy, we identified and quantified 11 cannabinoid compounds present in the polar CSCE that individually exhibit significant efficacy in inducing cell death in GBM tumor cells. Conversely, the polar fraction in our experiment did not demonstrate efficacy against U570 cells.

Conclusion

The ability to quantify individual compounds within a cannabis extract that selectively induces cell death in brain tumors holds promise for future research and the potential development of standardized therapy for patients with GBM.

Introduction

Anxiety is a natural response to real or perceived danger or threat to one's security. The fifth edition of the *Diagnostic and Statistical Manual for Mental Disorders* lists disorders related to anxiety that include general anxiety disorder (GAD), post-traumatic stress disorder (PTSD), and sleep disorder, among others (eg, dementia, alcohol use disorder, opioid use disorder).[1] GAD is defined as excessive worry or apprehension that persists for at least 6 months.[1] Depression is often defined as a mood disorder with feelings of hopelessness and sadness that are persistent.[1] The 2014 Canadian clinical practice guidelines for the management of anxiety, PTSD, and obsessive-compulsive disorders report the worldwide lifetime prevalence of anxiety and related disorders to be as high as 31%.[2] Patients with anxiety and related disorders are also at an increased risk for developing a comorbid major depressive disorder, resulting in reduced quality of life primarily due to functional impairment.[2]

Statistics Canada has published findings showing that in 2013,   an estimated 3 million people in Canada over the age of 18 self-reported a mental health problem or illness.[3] Of this population, 23% who felt they were experiencing anxiety or depression had never consulted a physician for their symptoms.[3] People who have been prescribed antidepressants often experience the emergence of discontinuation symptoms upon stopping medications.[4] Although data show clinical improvement of anxiety with prescription medications, a large 2017 cross-sectional study looked at the effects and benefits of substituting cannabis for prescription medications for therapeutic purposes.[5] This study reported that 46% of patients (N=2774) used cannabis as a substitute for prescription drugs. Self-reported medical users were 4.5 times more likely to report substituting cannabis for their medications, while up to 25% of nonmedical users also reported substituting cannabis for prescribed drugs.[5]

Because recreational use of cannabis was legalized by the Canadian federal government in 2018, stigma related to cannabis use has declined,[6] and interest in cannabis use for medicinal purposes has increased.[7] According to a Canadian Cannabis Survey in 2022, 13% of Canadians older than 16 reported having used cannabis for medical purposes, and 73% did not have authorization from a health care professional.[8] The role of cannabis in alleviating anxiety has been attributed to cannabidiol (CBD), an active cannabinoid.[9] However, the current evidence supporting this claim is of low quality—in terms of the experimental design and reliance on animal data.[10] Conversely, another major active ingredient in cannabis, delta-9 tetrahydrocannabinol (THC), has been shown to produce symptoms of anxiety at higher doses.[10] Although anxiety is one of the most commonly reported reasons for cannabis use, along with other comorbid conditions such as depression, pain and stress,[11] its anxiolytic effects are not always consistent due to differences in cultivars (eg, THC:CBD ratios,[12] levels of other active compounds, such as terpenes) as well as differences in dosing and frequency. This area of cannabis research requires further investigation.

To contribute to the available literature and medical understanding of the impact that medical cannabis has on anxiety and related disorders, we conducted a retrospective review of patients who received their medical cannabis documentation and authorization from Harvest Medicine (HMED)—a network of multidisciplinary medical cannabis clinics in Canada.

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Methods

A retrospective chart review was conducted to examine medical cannabis use in adults who self-reported anxiety as one of their primary mental health/psychiatric disorders in an electronic intake questionnaire for seeking cannabis therapy at the HMED clinics from May 2017 to July 2021. Specifically, the study assessed the impact of medical cannabis on anxiety and depression levels as scored on the General Anxiety Disorder-7 (GAD-7) and depression, as a comorbidity, as scored on the Personalized Health Questionnaire-9 (PHQ-9). HMED is a Canadian network of specialty medical cannabis clinics owned by MediPharm labs with locations across Canada. Clinic locations in Edmonton, Calgary, Cole Harbour, and Moncton offer both in-person and telemedicine appointments. HMED's electronic health records with structured assessment tools were used to capture all patient data retrospectively. The study protocol was approved by the Children's Hospital of Ontario (CHEO) Research Ethics Board.

Inclusion criteria

All medical cannabis HMED patients who self-reported anxiety as one of their mental health conditions in an electronic baseline questionnaire were included. Additionally, all patients with demographic data that included a first follow-up assessment separated from the baseline appointment by more than 7 days and all patients with a GAD-7 score >4 were included.