Medical Cannabis Treatment in Patients with Glioblastoma Multiforme

A Retrospective Cohort Study

Laszlo Mechtler MD, FAAN, FEAN, FASN, FAHS, Christopher Ralyea Jr., MBA, Paul Hart MA, Vincent Bargnes BS, Alexander Benyovszky, MD

DENT Neurologic Institute Buffalo, NY, USA

Poster ID: 4639

Objective & Study Design

Objective

The purpose of this study is to assess medical cannabis' (MC) efficacy on survival rates, quality of life, and adverse effects in patients with pathology-confirmed Glioblastoma Multiforme(GBM).

Study Design

42 patients with pathology-confirmed Glioblastoma Multiforme were followed at an outpatient, tertiary neurologic facility in Buffalo, NY, USA. Out of the 42 patients, 23 utilized MC through New York State's Medical Marijuana program. Patients utilized MC from a NYS dispensary for at least 1 month. Electronic health records of MC certified patients were reviewed for the following information: patient-reported efficacy, MC dosing, opioid pain medications, seizure medications, steroids and Adverse events (AE's) which was then analyzed for this study. Survival and quality of life outcomes were compared to the matched control group, including pathology grading and tumor genotype, who were not exposed to MC.

Inclusion/ Exclusion

- Certified for New York State MC by UCNS board certified physicians or their nurse practitioner/physicians assistant team.
- Patients were on MC for at least one month treatment
- At least 21 years of age

Subjects

- 23 patients diagnosed with GBM and were certified for MC
- 60.87% were female, 39.13% were male
- 19 patients diagnosed with GBM and were not using MC were compared to as the control group.

Study Population

- 42 patients met inclusion criteria, of which 23 were in the MC cohort and 19 were in the control cohort.
- Reasons for failure to initiate MC treatment included:
  - Financial barriers
  - Employment restrictions

Approved by the Western Institutional Review Board (WIRB)

Results

Figure 1.

Study participants in MC and control cohorts by Sex

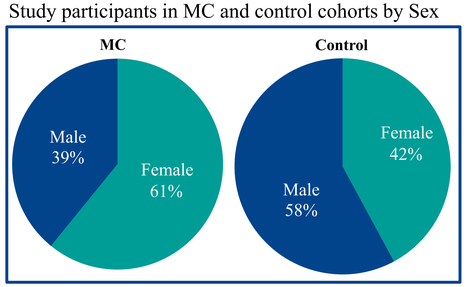
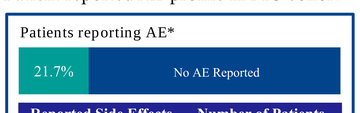


Figure 2.

Patient reported AE profile in MC cohort



Reported Side Effects	Number of Patients
Anxiety	1
Cognitive Impairment	1
Less Ambitious	1
Lethargy	1
Seizure	1
Taste	1

*13% discontinued due to AE. No severe AE.

Figure 3.

Comparison of medication reduction reported between MC and control group

	MC Cohort		Control Cohort	
Medications	% patients reporting dose reduction	% patient reporting discontinuation	% patients reporting dose reduction	% patient reporting discontinuation
Steroid	55.56%	44.44%	30.77%	7.69%
Opioid	100%	50.00%	50.00%	50.00%

Results

Figure 4.

THC:CBD ratios (all products in MC group)

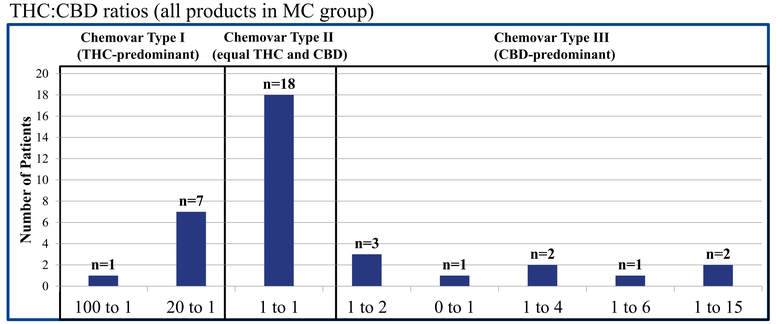


Figure 5.

Self-reported improvement in MC group

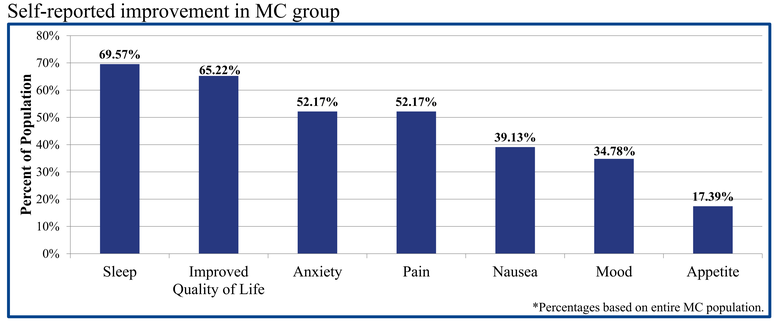
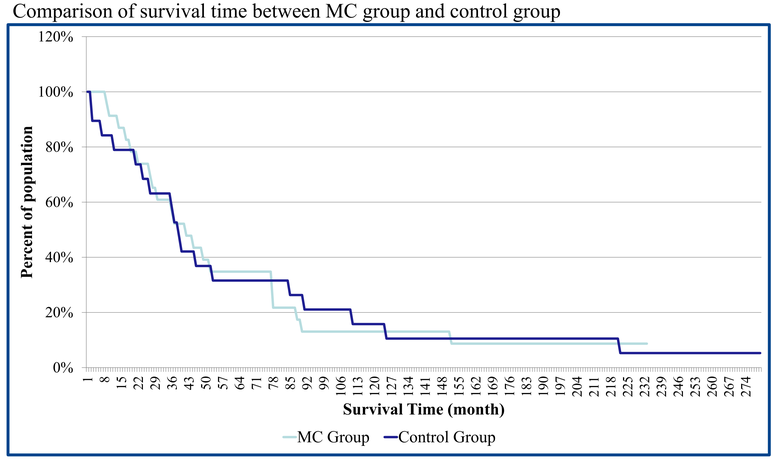


Figure 6.

Comparison of survival time between MC group and control group



Discussion

The results of this study suggest physicians should consider incorporating MC as a complementary treatment plan of those patients diagnosed with GBM to improve their quality of life (QOL). There was no significant difference observed in the median survival time between patients with GBM utilizing MC (M=63.6 months; SD=63.5 months) and the matched control group (M=65.8 months; SD= 74.5); p = 0.91. Average MC exposure was 9.34 ±8.50 months in the 23 patients utilizing MC (median age 53 years, 61% female, 30% reporting previous cannabis use.) Patient-reported improvements were most notable in sleep(70%), overall quality of life(65%), and anxiety(52%). The most common used products were Type II chemovar (equal tetrahydrocannabinol to cannabidiol ratio), this was associated with the reported improvement while minimizing AE reporting.

Certain preclinical trials suggest that compounds found in cannabis have chemotherapeutic effects, including THC and CBD. THC can induce human glioma cell death through induction of autophagy. CBD can inhibit cell invasion by glioblastoma cells. The defects in the TP53 and PTEN genes of patients with GBM do not protect glioma cells from cannabinoid-induced cytotoxicity in pre-clinical animal trials. These effects were not observed to increase survival time in the clinical setting. While MC did not provide appreciable chemotherapeutic effects, MC did improve the quality of the remarkable limited survival time following GBM diagnosis for over 65% of patients. Effects were most notable for sleep, anxiety, and pain improvement.

MC is largely tolerated by participants, with no serious AEs. Of patients utilizing MC, 21.7% reported side effects from MC, with 13% discontinuing MC due to AE. However, the absence of comprehensive professional guidelines surrounding MC for GBM forces physicians to practice within a large clinical evidence gap or to avoid both risks and benefits associated with MC. Further studies are required to investigate the role of MC in comprehensive GBM treatment plans.

Conclusion

This study suggests that there is no association between improved survival rate of GBM and MC treatment. MC may be implemented as complementary treatment plans for the improvement of QOL, including sleep and anxiety. Further randomized, placebo-controlled studies are needed to investigate such associations with an emphasis on improving the QOL and survival outcomes for patients with GBM.

Acknowledgements & References

This study was supported by The Harry Dent Family Foundation, Inc. a 501(c)(3) non-for-profit organization dedicated to supporting neuroscience research. Special thanks to all of the patients within the study and the staff at DENT Neurologic Institute.

Ellert-Miklaszewska, A.;Ciechomska, I.A.; Kaminska, B. "Synthetic Cannabinoids Induce Autophagy and Mitochondrial Apoptotic Pathways in Human Glioblastoma Cells Independently of Deficiency in TP53 or PTEN Tumor Suppressors. "*Cancers 2021*, 13, 419.

Ivanov, V. N., Grabham, P. W., Wu, C. C., & Hei, T. K. (2020). Inhibition of autophagic flux differently modulates cannabidiol-induced death in 2D and 3D

Lah, T.T.;et al. "Cannabigerol Is a Potential Therapeutic Agent in a Novel Combined Therapy for Glioblastoma." *Cells 2021*, 10, 340.

Salazar, M.;et al. "Cannabinoid action induces autophagy-mediated cell death through stimulation of ER stress in human glioma cells." J. Clin. Investig. 2009, 119, 1359–1372.

Solanki, C., Sadana, D., Arimappamagan, A., Rao, K. V. L. N., Rajeswaran, J., Subbakrishna, D. K., ... & Pandey, P. (2017). Impairments in quality of life and cognitive functions in long-term survivors of glioblastoma. Journal of neurosciences in rural practice, 8(2), 228.

Steele, G., Arneson, T., & Zylla, D. (2019). A comprehensive review of cannabis in patients with cancer: availability in the USA, general efficacy, and safety. Current oncology reports, 21(1), 10.

Author Disclosures:

Dr. Mechtler: Advisory board appointment, speakers bureau participation, and/or research support from the following: Amgen, Avanir Pharmaceuticals, Biohaven Pharmaceuticals, Boston Biomedical Inc., CellDex Pharmaceuticals, Delmar Pharmaceuticals, electroCore, Novartis, Orbis Pharmaceuticals, Promius Pharma, Teva Pharmaceuticals, The Harry Dent Family Foundation, Inc. Dr. Mechtler also reports being the Medical Director/Consultant for Jushi, Inc.

All other authors report no disclosures.