Cannabis in the Treatment of Motor Neuron Disease

A Retrospective Study

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Background

With medical cannabis (MC) legalized in 38 states and the District of Columbia, it has become a growing subject of discussion in recent years. The endocannabinoid system (ECS) is known to be heavily involved in different neurological disorders, suggesting that MC's interactions with the ECS may play a role in treating these disorders. As a result, research on it's impact on these disease states, including ALS and other motor neuron diseases (MND), has expanded.

MND's are defined as a group of progressive neurological disorders that affect motor function. The current common FDA-approved drugs used to moderate effects of progression and increase survival time on MNDs include Riluzole and Edaravone. With over 30,000 active cases, $279-472 million being spent annually on treatment in the United States alone, as well as fatality being typical within 5 years of diagnosis, researchers have been searching for further treatment measures to combat these diseases. Consequently, with the known benefits of MC and its impact on the comorbidities of such disorders, it has emerged as a potential treatment option to slow the rate of disease progression and improve quality of life (QOL) in these patients.

Objective & Study Design

Objective

The purpose of this study is to examine MC as a treatment option for motor neuron diseases (MND)

Study Design

This is a retrospective study where 81 patients with a confirmed motor neuron disease were followed at an outpatient, tertiary neurologic facility in Buffalo, NY, USA. Out of the 81 patients, 33 met the inclusion/exclusion criteria and utilized MC through New York State's Medical Marijuana program with at least one month of use. Electronic health records of MC-certified patients were reviewed for the following information: patient-reported efficacy, Adverse events (AE's), MC dosing, medications, BMI, and ALSFRS-R scores which were compared to case-matched controls whom did not receive MC therapy.

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

- 81 patients diagnosed with MND and were certified for MC
- 228 patients diagnosed with MND and were not certified for MC
- 33 of the 81 patients met the inclusion criteria and were included in the study
- 64% were male and 36% were female in MC group and control group

Study Population

- 33 patients were included in the MC group
- 33 patients were included in the control group
- Reasons for failure to initiate MC treatment included:
  - Financial barriers
  - Employment restrictions

Results

Figure 1. THC:CBD ratio by visits

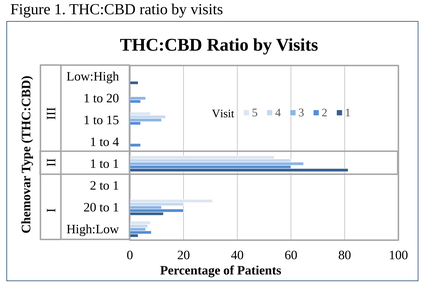
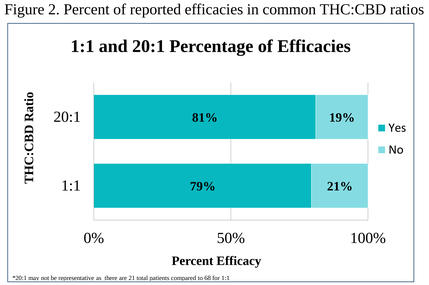


Figure 2. Percent of reported efficacies in common THC:CBD ratios



Results

Figure 3. MC and Control demographic

Population Characteristics	Control	MC
Mean Age At Treatment Start, Years	59 (±12)	59 (±12)
Male	21 (64%)	21 (64%)
Female	12 (36%)	12 (36%)
Caucasian	21 (64%)	25 (76%)
History of Recreational Cannabis Use	0 (0%)	4 (12%)
MND Type	Control	MC
Amyotrophic Lateral Sclerosis (ALS)	31 (93%)	24 (73%)
Primary Lateral Sclerosis	0 (0%)	4 (12%)
Unspecified MND	1 (3%)	3 (9%)
Other	1 (3%)	2 (6%)
History of Mental Health	Control	MC
No	17 (52%)	16 (48%)
Yes	16 (48%)	17 (52%)
Depression and Anxiety	5 (15%)	7 (21%)
Anxiety	6 (18%)	6 (18%)
Depression	5 (15%)	4 (12%)
Inclusion Overview	**Control**	**MC**
Total Patients with MND Diagnosis (not MC certified)	228	81
Total Patients Excluded	195	48
Total Patients Included	33	33

Figure 4. ALSFRS-R scores in MC vs. Control group

ALSFRS-R Category	MC Cohort	Control Cohort	p-value
ΔSpeech	-0.89	-0.95	0.968
ΔSalivation	-0.37	-0.05	0.857
ΔSwallowing	-0.10	-0.62	0.300
ΔHandwriting	-0.60	-1.40	0.067
ΔCutting food	-0.44	-1.45	0.017
ΔDressing & Hygiene	-0.37	-1.45	0.002
ΔTurning in Bed	-0.30	-1.00	0.116
ΔWalking	-0.80	-1.10	0.322
ΔClimbing Stairs	-0.50	-1.90	0.003
ΔDyspnea	-0.38	-1.07	0.219
ΔOrthopnea	-0.31	-0.85	0.211
ΔRespiratory Insufficiency	-0.43	-0.36	0.873
ΔTotal ALSFRS-Score	**-4.63**	**-10.14**	**0.024**

Figure 5. Comparison of survival time in the MC and Control groups

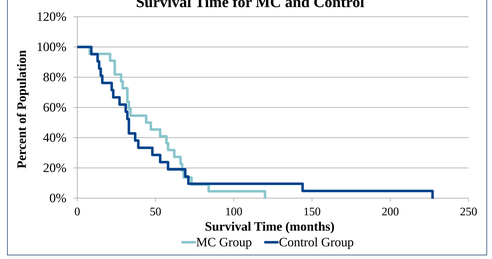


Figure 6. Comparison of BMI progression

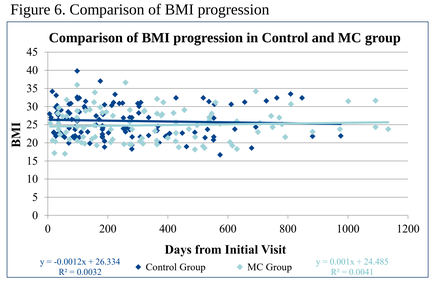


Table 1. Discontinuations of medications between MC and Control

Medications	MC Cohort: Percent of patients reporting discontinuation*	Control Cohort: Percent of patients reporting discontinuation*	p-value
Edaravone	45.45%	0.00%	0.016
Riluzole	31.82%	9.09%	0.025
Opioids	18.18%	0.00%	0.436
Benzodiazepines	42.86%	0.00%	0.042

* Percentage based off number of patients in the study

Figure 7. Number of self-reported AEs

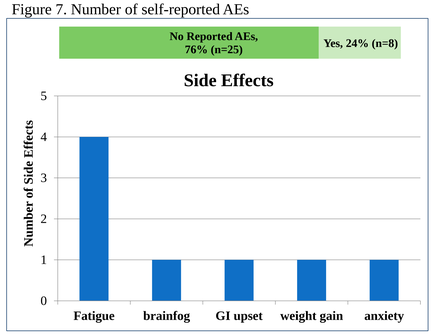
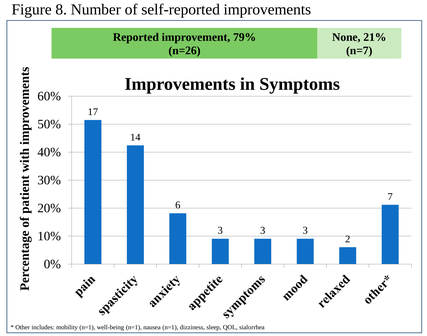


Figure 8. Number of self-reported improvements



Discussion

These results suggest that MC treatment for MNDs can have positive impacts on the patients' disease state, and should be considered by physicians as part of a comprehensive care plan. Of the 33 patients included in the treatment group, 79% reported symptomatic improvement with the use of MC. This was most prevalent in alleviating pain 52% (17), spasticity 42% (14), anxiety 18% (6), which are all common comorbidities of MNDs. MC therapy also allowed for the discontinuation of traditional MND medications (p=0.004). These included statistically significant reductions in Riluzole (p=0.025), Edaravone (p=0.016), as well as Benzodiazepines (p=0.042) in the MC group in comparison to the control. In the MC group, the BMI did increase slightly throughout the study. An increase in BMI is associated with reduced risk of mortality in ALS patients. It's reported those with overweight (BMI ≥ 25 kg/m^2) and obese patients (BMI ≥ 30 kg/m^2) have a 35% to 54% reduced risk of mortality when in comparison to patients with BMI < 25 kg/m^2. Although the BMI did increase in the MC group, this change was not significant (p=0.93). It is worthy to note that the starting BMI for MC group was lower than the control group, indicating that the MC group may have been further along in progression of the disease which could impact the results. Consequently, this study may not have accurately captured these effects due to the nature of the study. Nonetheless, these promising findings promote a longer study to be implemented with a larger sample size to further assess these results.

The MC group also displayed a statistically significant difference from the control group in ALSFRS-R score decrease (p=0.024). This was especially prominent in the areas of food cutting (p=0.017), dressing (p=0.002), and climbing stairs (p=0.003). This indicates that the rate of deterioration of motor neuron function in the MC group was slower when compared to the control in these realms of activities. The survival rate for the patients were also evaluated. When analyzed, the median survival rate of the MC group (M=33.0 months from symptom onset) compared to the control (M=33.0 months from symptom onset) did not change significantly (p=0.91).

The average exposure of MC was for 19.3 (±17.0) months. The most common product modality used was a 1:1 THC:CBD ratio (chemovar type II) administered via oral tincture, with an average total daily dose exposure of 12.4mg:14.6mg. Of those who utilized the 1:1 ratio, 79% reported efficacy of the product. MC was also shown to be largely tolerable by the patients. Of those included, only 24% (8) reported adverse effects (AE) and 9% (3) discontinued treatment due to the AEs. The most prevalent of these was fatigue at 12% (4). However, as the treatment progressed, the noted AEs were largely resolved.

Limitations of the study include selection bias as well as information bias due to being a retrospective study. This study also utilizes a small sample size, therefore the results may not be representative of the population. Nonetheless, with MC being administered in this study and showing a significant decrease in the use of MND drugs such as Riluzole and Edaravone, it's plausible to see MC as a viable treatment option for ALS onset. Although these results are promising, further large scale prospective trials are necessary to further evaluate the effects of MC on MNDs.

Conclusion

MC may be utilized in a comprehensive care plan for MND for the improvements of QOL, including pain, spasticity, anxiety, and mood. It use may also can result in discontinuation or reduction of other MND medications such as Riluzole, Edaravone, and Benzodiazepines.

The findings suggest that MC may slow MND progression as evidenced by the slower rate of decline in the ALSFRS-R scores.This study suggests that there is no association between improvements in survival rate or BMI in the MND patients with MC treatment.

Overall, the results of this study are encouraging for patients and providers alike. Given the retrospective nature of this study and relatively small sample size, larger prospective trials are needed to further validate MC therapy in the treatment of MND

Acknowledgements & References

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