Medical Cannabis as an Adjunctive Treatment for Epilepsy

A Retrospective Study

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Background

Medical cannabis (MC) has grown as a topic of discussion in recent years due to it's implication on a variety of neurological disorders. As a result, research on it's impact pertaining to states such as epilepsy is rising. Epilepsy is a chronic non-communicable diseases of brain that affects 50 million people worldwide and can be fatal. It's described as a neurological disease that causes recurring seizures. The CDC states that there are around 3.4 million people with active epilepsy, over 5.1 million people in the United States that have a history of epilepsy, as well as $8.6 billion being spent annually on it's treatment.

There are a multitude of approved pharmaceutical interventions to treat this disorder including Levetiracetam, Clonazepam, Gabapentin and Epidiolex. However, none of the present therapies provide complete resolution for all patients as such researchers continue to look for new treatments. Cannabis, specifically, cannabidiol (CBD), has shown potential to help reduce the severity and frequency of seizures in individuals with epilepsy. Results from recent clinical trials have supported MC as a treatment for epilepsy but have fallen short of providing complete resolution.

Objective & Study design

Objective

The purpose of this study is to provide insight into how medical cannabis (MC) can be used as an alternative treatment to epilepsy differing from the traditional medications

Study Design

This is a retrospective study where 479 patients with confirmed epilepsy were followed at an outpatient, tertiary neurologic facility in Buffalo, NY, USA. Out of the 479 patients evaluated, 132 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 for MC certified patients were reviewed for the information. Patients were advised of and agreed to sign the cannabis clinic consent form. Patients were trialed on different dosages pertaining to their specific needs. Patients were monitored over the course of their treatment

Patients included	
Baseline	132 patients
V1	132 patients
V2	103 patients

Inclusion Overview & Population Characteristics

Inclusion/Exclusion

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

Subjects

- 479 total patients were certified for MC, 132 were included in the study, and 347 were excluded.
- Of included patients, 58 (44%) were male, 74 (56%) were female, ranging from 6 to 83 years of age.
- The average age was 40 years old, with a standard deviation of 19.62 years.

Study Population

- 132 patients met inclusion criteria and initiated MC treatment.
- Reasons for failure to initiate/continue NYS MC treatment included:
  - Financial barriers
  - Failure to register through NYS
  - Purchased from another state
  - Stopped prior to first follow-up

Results

Figure 1. Prior cannabis use

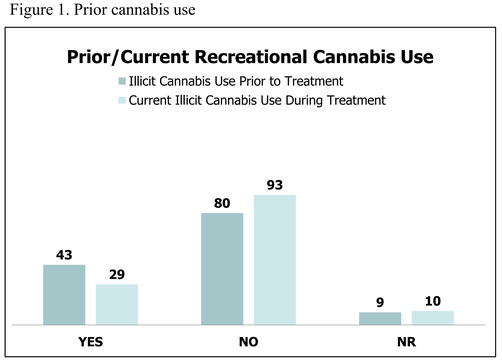

Table 1. Ratios and Modality

THC:CBD Ratio	N (%)
20:1	26 (20%)
1:1	66 (50%)
1:20	25 (19%)
Mode of Consumption	**N (%)**
Oral Tincture	107 (81%)
Vaporizer	27 (20%)
Capsule	15 (11%)

*Some patients started with multiple products, e.g. both a tincture and a vaporizer

Results

Table 2. Change in Monthly Seizure Activity

Visit	Average # of seizures per month	% change from baseline
Baseline	36.63	
V1	30.72	-16.13%
V2	25.33	-30.85%

*Seizure Activity was self reported and witness reported. Average # of seizures includes all subtypes reported by patients.

Figure 2. Improvement of Symptoms

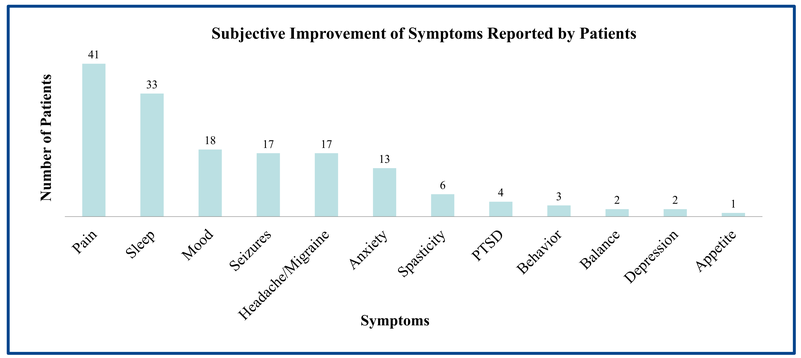

Table 3. Change in Anticonvulsants

Change in Anticonvulsants		
Visit	Average total # of ASD'S taking	Mean percent change
Baseline	1.73	
V1	1.69	2.31%
V2	1.66	4.05%

Table 4. Change in AEDs from baseline

% of patients able to reduce consumption			
AED	Baseline	Visit 1	Visit 2
Gabapentin	17	5.88%	17.64%
Lamotrigine	37	8.11%	24.32%
Carbamazepine	4	0.00%	50.00%
Oxcarbazepine	9	88.89%	0.00%
Phenytoin	9	0.00%	33.33%
Zonisamide	11	27.27%	27.27%
Levetiracetam	55	-6.64%	30.91%
Topiramate	13	15.38%	23.1%
Valproic Acid	28	7.14%	17.86%
Vimpat	17	5.88%	5.88%
Phenobarbital	9	11.11%	55.56%

Table 5. Change in Benzodiazepines from baseline

% of patients able to reduce consumption			
Benzodiazepine	Baseline	Visit 1	Visit 2
Clonazepam	37	2.70%	24.32%
Lorazepam	15	0.00%	13.33%
Diazepam	10	-10.00%	10.00%
Onfi	12	50.00%	41.66%
Alprazolam	4	0.00%	50.00%
Midazolam	6	-16.67%	0.00%
Diastat	11	-18.18%	0.00%

*Certain ASD's and Benzodiazepines not included in baseline charts if less than 4 patients were taking at baseline

Table 6. Other Medication Changes

	# of patients	% of reductions	p-value
Decrease in opioid	9	45.00%	0.011
Discontinuation of opioid	9	45.00%	0.011
Decrease/discontinuation in benzodiazepine	12	16.43%	0.416

*These results are based off the number of patients consuming a particular class of drug. Patients may consumes more than one drug from the same class. All values are relative to baseline.

Table 7. THC:CBD mg exposure

THC:CBD mg exposure		
Visit	Average THC mg per day	Average CBD mg per day
V1	12.45	23.38
V2	14.39	27.79

Table 8. Adverse Effects

Adverse Side Effects:	N (%)
Sedation	8 (6%)
Anxiety	3 (2%)
Increased Appetite	6 (5%)
Dizziness	5 (4%)
Nausea	5 (4%)
Cognitive Impairment	4 (3%)

*No severe adverse events were reported

Discussion

These results indicate that MC may have positive implications for those suffering from epilepsy as well as it's comorbidities and can be used in a comprehensive care plan by physicians. Of the 132 patients included 104 (79%) reported efficacy in at least one domain. The most noteworthy are in pain 41 (31%), sleep 33 (25%), mood 18 (14%), and seizures 17 (13%). At a minimum, this data supports the use of MC for the mitigation of symptoms in those suffering from epilepsy. In addition to symptomatic benefit MC appears to be well tolerated by this patient population. While 28 (21%) patients reported adverse events (AE), with the most common being sedation 8 (6%) no SAEs were reported and no patients discontinued treatment as a result. Marked reductions in pharmaceuticals often prescribed to this patient population were also recorded. As a result of MC treatment, many were also able to reduce or discontinue other typical pharmaceutical interventions used to treat epilepsy. These treatments include anticonvulsants as well as benzodiazepines, however, these reductions were not statistically significant with respect to medication classes. There were however statistically significant decreases in specific medications including opioids which saw a 45% discontinuation rate.

Perhaps even more important was the decrease in average monthly seizure activity. With decreases from baseline at visit 1 and visit 2 at 16.13% and 30.85% respectively. This result indicates that MC therapy may offer additional therapeutic benefits to one's existing treatment regimen. The average daily dose exposure of THC and CBD to achieve these results were 12.45mg:23.38mg and 14.39mg:27.79mg at visits 1 and 2 respectively. This is equivalent to approximately a 1:2 ratio. The most common route of administration was via oral tincture with the vast majority of the patients reporting no prior cannabis use.

Limitations of the study include selection bias and information bias due to the nature of it being a retrospective study.

Conclusion

Study results indicate MC may be utilized in a comprehensive care plan for the treatment of epilepsy and common comorbidities including but not limited to pain, seizures, anxiety, mood, and sleep. Its use may also facilitate reduction and/or discontinuation of typical pharmaceutical interventions prescribed to epileptics such as anticonvulsants and benzodiazepines, as well as opioids. The findings suggest that MC therapy may decrease monthly seizure frequency with a favorable side effect profile.

In a departure from previous studies, this data suggests that decreased seizure activity can be achieved without the utilization of high CBD ratios, in fact these results were achieved with an approximate THC:CBD ratio of 1:2. While this study does not replace large-scale placebo-controlled trials its results are encouraging and add to a substantial line of inquiry.

Acknowledgements & References

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