Outcomes Among Opioid Users Enrolled in the New York State Medical Marijuana Program

Dr. Ranga Krishna MD, Erica Glants, Eric Hirsch MS4

Disclosures: None

Conflicts of interest: None

History of Medical Marijuana

2300 BC: First documented for its medicinal uses in China. Used as a form of anesthetic and in treating pain from menstrual cramps

1830: Irish doctor Sir William Brooke O'Shaughnessy found cannabis extracts reduced stomach pain and vomiting in people with cholera.

1850-1937: Cannabis referenced in the *United States Pharmacopoeia* and widely utilized as a medicine.

1937: Federal restriction of cannabis use through Marijuana Tax Act.

1970: Classified as Schedule 1 drug, restricting further research.

1996: California becomes first state to permit medical access though Compassionate Use Act.

The Endocannabinoid System (ECS)

❖ Role in homeostasis
❖ Has been characterized as the "eat, sleep, relax, forget, and protect" system.

The ECS Controls:
- Appetite
- Stress
- Memory
- Pain

Marijuana contains over 113 cannabinoids

The two most recognized cannabinoids are Tetrahydrocannabinol (THC) and Cannabidiol (CBD)

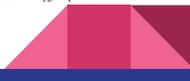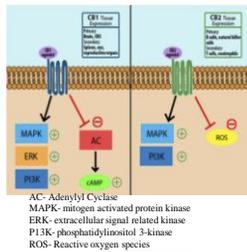## Endocannabinoid Receptors

Two Primary Receptors:

CB1 - found in CNS
CB2- found in peripheral tissues

AC- Adenylyl Cyclase
MAPK- mitogen activated protein kinase
ERK- extracellular signal related kinase
P13K- phosphatidylinositol 3-kinase
ROS- Reactive oxygen species

Anandamide

First endocannabinoid discovered

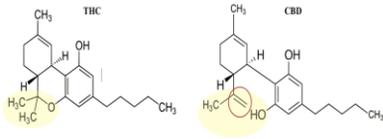Synthesized in our bodies

Controls:
- Pleasure
- Mood stabilization
- Anxiety reduction
- "Runners High"

If THC binds instead,
- Impaired cognition
- Short term memory loss
- Drowsiness
- Hunger stimulation
- Anxiety

Chemical Components: THC and CBD ($C_{21}H_{30}O_2$)

- Structural differences result in significant differences in binding
- CBD is referred to as negative allosteric modulator of the CB receptor

State Medical Marijuana Programs

There are currently 23 active state medical marijuana programs accepting patients with physician-confirmed diagnoses.

Eligible diagnoses vary by state, but usually include the following:
- **Chronic/Neuropathic Pain (up to 90% of patients)**
- Depression/Anxiety
- Neurodegenerative Disorders(MS, ALS, Parkinsons, ETC)
- Cancer
- HIV/AIDS
- IBS/Crohns
- PTSD

Prescription

1) Patients are evaluated by a licensed medical marijuana provider for authorization
2) Upon acceptance, patients apply for their identification card
3) Patients bring identification card to licensed dispensaries.

Dosing

-Inhalation (through a vaporizer)

-Oral Tinctures (Oil held under the tongue, and then swallowed)

-Pills

-Edibles

THC LEVEL	CBD LEVEL	RATIO
None	HIGH	0:1
LOW	HIGH	1:20
1 OR EQUAL	1 OR EQUAL	1:1
HIGH	LOW	20:1 or 50:1

Medical Marijuana Today

❖ Approximately 25 million Americans use medical marijuana monthly

❖ A recent Quinnipiac University poll concluded 54% of American voters favor the legalization of recreational cannabis, while 81% of respondents favor medical use.

New York State Medical Marijuana Program

❖ With the signing of the Compassionate Care Act on July 7th, 2014, New York became the 23rd state to allow it for medical use.

❖ As of May 2019, the Medical Marijuana Data Management System (MMDMS) has registered 2,348 practitioners and 100,559 certified patients.

Role in Chronic Pain

❖ A 2017 report by the US National Academies of Science, Engineering, and Medicine, which analyzed more than 10,000 studies, found "strong evidence" that marijuana is useful in treating chronic pain."

❖ CB1 and mu opioid receptors (MORs) have significant overlaps in distribution (e.g. the periaqueductal gray, locus coeruleus nucleus accumbens)
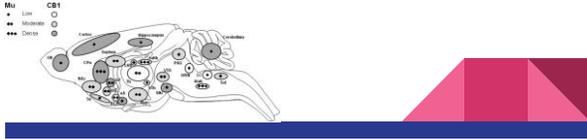
Methods

Data Collection

❖ Phone and in-person interviews were conducted with 139 patients (former and current) opioid users enrolled in the NYS Medical Marijuana Program under the diagnosis of chronic pain through a neurology clinic in South Brooklyn.

❖ All patients had been taking medical marijuana between 1 month and 1 year

❖ Doses ranged in ratios from Low to High in both CBD and THC

Data Collection (cont.)

Patients were asked the following questions:

1. What was your average daily pain level on a scale of 1-10 before and after starting medical marijuana therapy?
2. How has medical marijuana therapy affected your overall quality life?
3. What is your average monthly out-of-pocket cost for medical marijuana?
4. How difficult is it to access the dispensary?
5. Are you still participating in the program and adherent to your regimen (defined as filling >80% of their prescriptions)?
6. Factors associated with dropping out/non-adherence?
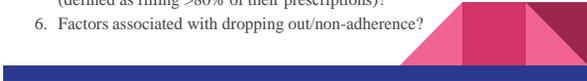
Results

Efficacy

❖ Almost all participants (138/139) reported alleviation of symptoms and improved quality of life.
❖ The average pain score decreased from 7.99 to 3.76

*One patient with phantom limb pain initially experience a 40% reduction of symptoms but subsequently developed rebound pain worsened by ingestion of the marijuana

6

Adherence

- ❖ A large number of participants, 58/139 (42%), either dropped out of the program or were no longer adherent to their treatment regimen.
- The majority of these patients (56/58) stopped taking marijuana primarily due to high out-of-pocket cost, which was $179 monthly on average.

- ❖ A large number of participants 43/139 (31%) also reported that accessing the dispensary was "hard" or "not easy."

Discussion

Marijuana and Chronic Pain

- ❖ More than 100 million American suffer some form of chronic pain
- ❖ Total cost of treatment estimated to range from $560 to $635 billion yearly

The "Opioid Epidemic"

❖ Although representing less than 5% of the world's population, Americans consume 80% of all opioids
❖ 2.6 million Americans suffer from opioid addiction
❖ Every day, more than 130 people in the United States die after overdosing on opioids

Opioid Epidemic (cont.)
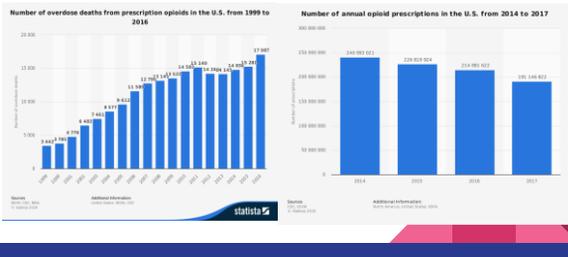
Medical Marijuana and Opioids

❖ The overlapping expression of CB1 and MOR provides a clear mechanistic rationale for MM in opioid use disorder.
❖ When given access to medical CBD, individuals currently using opioids for chronic pain decrease their use of opioids by 40–60% and report that they prefer CBD to opioids.
❖ Patients in these studies reported fewer side effects with cannabis than with their opioid medications and a better quality of life.

Systemic Effects

❖ A longitudinal analysis of Medicare PartD found that opioid prescriptions decreased by 2.11 million daily doses per year when a state instituted a medical cannabis law.
❖ Opioid prescriptions decreased by 3.742 million daily doses per year when an MM dispensary opened.
❖ Medical marijuana laws were associated with a mean 24.8% lower annual rate of opioid overdose deaths compared to state without such laws.

Barriers to Access

❖ Medical marijuana is not currently covered by insurance, burdening patients with high out-of-pocket costs

-Cited as the most most common reason for drop-out/non-adherence
-Previous study by the Drug Policy Alliance found that 77% of NYS MM patients were unable to afford their prescription.

❖ 85% of recent medical school graduates receive no education about cannabis throughout their training.

Schedule I

Schedule I drugs, substances, or chemicals are defined as drugs with no currently accepted medical use and a high potential for abuse. Some examples of Schedule I drugs are:

heroin, lysergic acid diethylamide (LSD), marijuana (cannabis), 3,4-methylenedioxymethamphetamine (ecstasy), methaqualone, and peyote

Drug Scheduling. Retrieved from https://www.dea.gov/drug-scheduling

Adverse Effects

❖ Acute: Impaired short-term memory, impaired motor coordination, altered judgment, paranoia, and psychosis (rare)
❖ Chronic Addiction, cognitive impairment, poor educational outcomes, chronic bronchitis and an increased risk of schizophrenia in individuals with strong risk factors.
❖ Vascular conditions, including myocardial infarction, stroke, and TIA, have also been associated with cannabis use in susceptible individuals.
❖ Wang et al. (2008) analyzed 31 studies found a total of 4,779 adverse effect, **96.6% (4,615) of these were not deemed by authors to be serious.**

Conclusions

❖ This study substantiates a growing body of literature that suggests marijuana can relieve symptoms and improve quality of life in patients with neuropathic pain.

❖ Our findings also underscore challenges associated with accessing medical marijuana under the current system.

❖ Without insurance coverage and a better system for distribution, the high out-of-pocket costs and logistical hurdles associated with medical marijuana will continue to limit access, disproportionately affecting low-income patients.

References

1. .Barber PA, Roberts S, Spriggs DA, et al. Adverse cardiovascular, cerebrovascular, and peripheral vascular effects of marijuana: what cardiologists need to know. Am J Cardiol. 2014;113:1086
2. Bradford AC, Bradford WD, Abraham A, Adams GB. Association Between US State Medical Cannabis Laws and Opioid Prescribing in the Medicare Part D Population. *JAMA Internal Medicine*. 2018;178(5):667. doi:10.1001/jamainternmed.2018.0266.
3. Bridgeman MB, Abazia DT. Medicinal cannabis: history, pharmacology, and implications for the acute care setting. Pharmacy and Therapeutics. 2017 Mar;42(3):180.
4. Darrell J. Gaskin, Patrick Richard. The Economic Costs of Pain in the United States. *The Journal of Pain*, 2012; 13 (8): 715 DOI: 10.1016/j.jpain.2012.03.009
5. Drug Policy Alliance. Assessing New York's Medical Marijuana Program: Problems of Patient Access and Affordability . June 2016. https://www.drugpolicy.org/sites/default/files/NY MMJ Implementation Report Q1 June 13 2016.pdf.
6. Evanoff AB, Quan T, Dufault C, et al. Physicians-in-training are not prepared to prescribe medical marijuana. Drug Alcohol Depend. 2017;180:151–155
7. Garin, J., Pohl, R. V., & Smith, R. (2018). The Effect of Medical Cannabis Dispensaries on Opioid and Heroin Overdose Mortality. *Available at SSRN 3270101*.
8. Karila L, Roux P, Rolland B, et al. Acute and long-term effects of cannabis use: a review. Curr Pharm Des. 2014;20:4112–4118.
9. McPartland JM, Duncan M, Di Marzo V, et al. Are cannabidiol and Δ9-tetrahydrocannabivarin negative modulators of the endocannabinoid system? A systematic review. Br J Pharmacol. 2014;172:737–753.
10. Medical Use of Marijuana Under the Compassionate Care Act: Two Year Report. *New York State Department of Health* . 2018. https://www.health.ny.gov/regulations/medical_marijuana/docs/two_year_report_2016-2018.pdf.
11. National Academies of Sciences, Engineering, and Medicine. The health effects of cannabis and cannabinoids: the current state of evidence and recommendations for research. National Academies Press: Washington, DC; 2017
12. Powell D, Pacula RL, Jacobson M. Do Medical Marijuana Laws Reduce Addictions and Deaths Related to Pain Killers? 2015. doi:10.3386/w21345.
13. Quinnipiac University. Allow marijuana for vets with PTSD, U.S. voters say 10-1, Quinnipiac University national poll finds; slim majority say legalize marijuana in general. Jun 6, 2016. [Accessed August 5, 2016].
14. Socias ME, Wood E, Lake S, et al. High-intensity cannabis use is associated with retention in opioid agonist treatment: a longitudinal analysis. *Addiction*. 2018;113(12):2250-2258. doi:10.1111/add.14399.
15. Wang T, Collet JP, Shapiro S, Ware MA. Adverse effects of medical cannabinoids: a systematic review. CMAJ. 2008;178:1669–1678.
16. Wiese, Beth, and Adrianne R. Wilson-Poe. "Emerging Evidence for Cannabis' Role in Opioid Use Disorder." *Cannabis and cannabinoid research* 3, no. 1 (2018): 179-189.

Questions?