Medical Cannabis a broad spectrum of (conflicting) effects

> And a bonus bit on the Nurse Practitioners role in the new law.

About MCANZ

- Started in 2016 in response to
 - Previous governments conservatism
 - Poor results of protests
 - Professionalism
- Aims include education, for the public and professionals.
- Main Agenda is price to patient for legal access.



Background, the problem of price

- Sativex costs approx. \$1000
- 1500mg of cannabinoids, equivalent to 15grams of raw cannabis
- 15grams (half an ounce) typically costs \$200
- As a temporary compassionate measure, patients requiring palliation have protection from the police.



Palliation Protections

Statutory defense

 Advanced – progressive - life limiting condition and "nearing" the end of life.

Nurse Practitioners can certify



CBD Declassification

- Previous National Govt created exemption to prescribe CBD. – It was still Class B
- Govt Bill accepts the UN findings of CBD, and is descheduling it entirely.
- Other Countries have CBD as a health food supplement, especially low doses. Still a Prescription Medicine



THE ENDOCANNABINOID SYSTEM

CB1

Receptors are concentrated in the brain & the central nervous system but are also present in some nerves and organs.

CB2

Receptors are mostly in peripheral organs, especially cells associated with the immune system.

TRVP1

Receptors are concentrated in the blood, bone, marrow, tongue, kidney, liver, stomach & overies.

TRPV2 Receptors are concentrated in the skin, muscle, kidney, stomach

& lungs.



GPR 18

Receptors can be found primarily in bone marrow, the spleen and lymph nodes, and to a lesser extend the testes

GPR55

Receptors are found in the bones, the brain, particularly the cerebellum, and the Jejunum and lleum.

GPR 119

Receptors are found predominantly in the Pancreas and the intestinal tract, in small amounts



/MCANewZealand/

MCAwarenessNZ

mcawarenessnz.org/

The plant itself

SATIVA

- + Tall in stature
- + Narrow leaves
- + Longer flowering cycles
- + Better suited for warm climates with a long season





INDICA

- + Short in stature
- + Broad leaves
- + Shorter flowering cycles
- + Suitable for colder climates with shorter seasons



Afghan Kush

Chemovars

Lemon strains : average terpene profiles



Entourage effect

- •Cannabinoids are more effective in combination
- •Animal study CBD inflammation
- Dosages in Epilepsy



CBD

CBC

CBN

THC

THCV

CBG

Psychoactivty

High THC

50:1-8:1

Mild THC

8.1-2.1 THC.CBD

THC negative effects modulated by CBD and other cannabinoids.

Pure THC

50:1+ THC:CBD

MILD CBD HIGH CBD 2.1-1.2 THC CBD 1:2-1:8 THC:CBD 1:8-1:50 THC-CBD

Balanced

PURE CBD

1:50+



Primary Cannabinoid THC

- Analgesic
- Anti emetic
- Anti Spasmodic
- Anti tumoral (high doses)
- Bronchodilator
- Lowers BP
- Increase Heart rate





Primary Cannabinoid CBD

- Anti Epileptic
- Analgesic
- Anxiolytic
- Anti tumoral (high doses)
- Bronchodilator
- Lowers BP
- Increase Heart rate





Primary Cannabinoid CBN

- Most Sedative Cannabinoid
- Analgesic
- •Anti Epileptic
- Less Pyschoactive than THC



CBN

Minor Cannabinoid CBG

- "Parent" Cannabinoid
- Obtained by harvesting early
- Appetite stimulant
- Particularly effective in animal model of IBD
- Inhibits colorectal cancer cells in mice
- Effective antibacterial agent, particularly MRSA



CBG

Minor Cannabinoid THCV

- Less euphoric than THC
- Inhibits euphoria and sedation of THC at low doses only.
- Found in African land race strains,
- Used in place of Ritalin as a nootropic in SA
 - Early studies suggest potential in insulin resistance in type 2 Diabetes
- Also potential in schizophrenia.



THCV

Main Uses

- Chronic pain approx. 60% of adult use
- Neurological conditions 18%
- Oncology 10%
- Other uses include for
- Inflammatory bowel disease,
- Wasting and appetite
- Anxiety and Depression.



Chronic Pain

- In adults with chronic pain, patients who were treated with cannabis or cannabinoids are more likely to experience a clinically significant reduction in pain symptoms. (1)
- With the possible exception of pain and spasticity in multiple sclerosis, there is little evidence for the effectiveness of cannabinoids in chronic non-cancer pain situations, whether or not the pain attracts the descriptor "neuropathic". (FPM 2015)





Cannabis Vs Opioids

- NON TOXIC
- Public health ramifications as an opioid substitute
 - 6 years after Medical Cannabis schemes enacted, 1/3rd reduction in Opioid deaths in US States. (2)
 - In Canada, 1/3rd of all drug substitution was Opioids(3)

Difficult to treat pain types.

- Neuropathic
- Sensitization disorders (4)



Opioid Synergies

 THC in part has analgesia via Delta and Kappa Opioid receptors(5)

> Synergestic effects varies with opioid 9.5 for codeine 3.6 for morphine

Does not significantly alter plasma opioid levels(6)

Research needed

" In summary, pre-clinical studies provide robust evidence of the opioidsparing effect of cannabinoids, whereas one of the nine clinical studies identified provided very-low-quality evidence of such an effect. Prospective high-quality-controlled clinical trials are required to determine the opioidsparing effect of cannabinoids." (7)



Cognition in Chronic pain

Recreational use linked to deficits in

- verbal memory
- Processing speed,
- Attention span and executive function

In CP however, a 3month follow up of new patients showed *improved measures(8)*, particularly

- executive function
- Sleep
- depression



Nausea and vomiting

There is conclusive or substantial evidence that cannabis or cannabinoids are effective Antiemetics in the treatment of chemotherapy-induced nausea and vomiting (oral cannabinoids) (9)

Regarded as more effective compared to pre mid 90s options, less than current options.

Higher adverse event rate (dizzy, high)

Secondary positive effects, (hunger, weight gain)

Emphasis on CINV, but historically HIV



Cannabinoid Hyperemesis

Paradoxical effect from overuse

Frequently misdiagnosed.

Similar to Cyclic vomiting syndrome,

Symptoms are relieved by hot showers

Ondansetron, metoclopramide, D2, H1 agonists ineffective (10)

Treatment options

Olanzapine 7.5mg ODT(11) Haloperidol Start IV up to 2mg, Then swap to Oral. Capsaicin topical

MCANZ has supported successful treatment with Haloperidol

Latest data suggest Olanzapine could offer some benefits over Haloperidol (11)

MENTAL HEALTH SUPPORT



Schizophrenia THC

- Data suggests Cannabis not a causation
- Cannabis does however, amplify pre existing, genetic link
- No correlation between population usage and incidence
- THC is the main culprit.
- THC may have positive short term calming effects in low doses

Usage rates in Schizophrenia high, potentially self medicating, seeking CBD, but getting the opposite....

Schizophrenia Genetics



Figure 3. Odds ratio (OR) of psychosis for *AKT1* rs 2494732 C/T or C/C carriers compared to subjects with the T/T genotype depending on lifetime frequency of cannabis use.

Schizophrenia - CBD

• CBD appears to be an antidote to psychosis

1000mg a day study showed

- Lower levels of positive psychotic symptoms
- Greater improvements in cognitive performance
- Considered less unwell by treating physician
- Similar adverse affects as placebo

CONCLUSION: These findings suggest that CBD has beneficial effects in patients with schizophrenia. As CBD's effects do not appear to depend on dopamine receptor antagonism, this agent may represent a new class of treatment for the disorder. (12)

Cannabis and Cancer risk

- Smoked Cannabis appears to be far less carcinogenic than tobacco
- Probably due to protective effects of cannabinoids
- Smoking still a problem, as it encourages tobacco use.
- There is modest evidence of increasing risk of testicular cancer (13)

Minimal evidence of use during pregnancy causing greater cancer risk in offspring (13)

CANNABIS VS CANCER

Cannabis and Cancer treatments

- Cannabinoids show selectivity in targeting some cancer lines in petri dish studies.
- Work by restoring apoptosis to cancerous cells
- Additionally inhibit the development of blood vessels to feed tumor.
- Other more technical cellular interactions (ICAM-1 etc) (14)
- Animal and early human trials show promise
- Higher doses (concentrates) required, tolerance and very high adverse effects. unlikely in a legal setting.
- Israel has defining research that remains unpublished.
- Preclinical data suggests different ratios optimal for differing tumor types.

Early Brain tumor research

- Cannabinoids densest in the brain
- Therefor antitumor effects likely to be exaggerated in the brain,
- Glioma leading test case for use.
- Spanish team circa 2006 started with Intracranial THC, well tolerated and showed effect
- 2011 Lab dish Temozolomide + THC showed enhanced effect

Sativex in Gliomblastoma Multiforme

- 12 sprays a day of Sativex in addition to Temozolomide
- Average survival of treated was 550 days,
- Untreated survival rate 369 days.
- Only 21 patients
- Imagine 100 sprays?



NZ Anecdote

- Elyse DIPG
- DIPG Survival rate less than 1% at 5 years
- Diagnosed 3 years ago
- 2 years past life expectancy
- Slight shrinking of tumor (1-2mm on each axis per quarter anum)
- 60mg of THC/CBD balanced oil, and unknown illicit oil



Questions?

References

- (1) <u>http://www.nationalacademies.org/hmd/~/media/Files/Report%20Files/2017/Cannabis-Health-Effects/Cannabis-chapter-highlights.pdf</u>
- (2) https://www.wolterskluwercdi.com/dental-newsletters/study-on-the-relationship-between-medical-cannabislaws-and-opioid-analgesic-overdose-deaths/
- (3) https://harmreductionjournal.biomedcentral.com/articles/10.1186/s12954-019-0278-6
- (4) https://www.ncbi.nlm.nih.gov/pubmed/17997224
- (5) https://www.ncbi.nlm.nih.gov/pubmed/14706563
- (6) https://www.ncbi.nlm.nih.gov/pubmed/22048225/
- (7) <u>https://europepmc.org/articles/pmc5520783</u> (8) <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5776082/</u>

(10) <u>https://www.the-hospitalist.org/hospitalist/article/175988/gastroenterology/treating-cannabinoid-hyperemesis-syndrome</u>

- (11) https://europepmc.org/articles/pmc5256592
- (12) https://www.ncbi.nlm.nih.gov/pubmed/29241357

(13) <u>http://www.nationalacademies.org/hmd/~/media/Files/Report%20Files/2017/Cannabis-Health-Effects/Cannabis-chapter-highlights.pdf</u>

(14) <u>https://www.cancer.gov/about-cancer/treatment/cam/hp/cannabis-pdq</u>