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Marijuana and ABI: Evidence and practice based considerations

Back to School Conference
Acquired Brain Injury Association
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Conflict of interest

- No COI to declare

Questions addressed

- Does cannabis have neuroprotective properties in ABI?
- Does medical marijuana help with post-ABI anxiety?
- Does medical marijuana help with post-ABI pain?
- What are the indications, precautions and contraindications, and dosing for medical marijuana?
- What are the psychiatric and social harms of marijuana?
- What are the clinical features and management of cannabis use disorder?

Does cannabis have neuroprotective properties after ABI?

- Nguyen 2014: 3 year retrospective study of 440 patients admitted to trauma unit with head injury
- 18% had positive toxicology screen for THC
- Risk of death was 2.4% for +ve screen versus 9.9% for –ve screen
- **Limitations**
- Mean age THC +ve vs -ve: 32 years vs 53 years
- Wide confidence interval: 0.051 – 0.991
- Alcohol +ve screen was also higher in THC group and other studies have shown association with alcohol and survival

Neuroprotective effects are probably not from THC

- Kwiatkoski 2011: Rats receiving cannabidiol had stronger recovery from spinal injury
- Dexanabinol and other cannabinoid analogues may reduce excitotoxic response, inflammation, vasospasm
- **Conclusion**:
- Further research needed on use of pharmaceutical cannabinoids in neuroprotection after ABI

Does medical marijuana help with post-ABI anxiety?

- Dr Carolyn Lemsky presentation to ABI 2013:
- ABI patients have high prevalence of anxiety and mood disorders:
  - Anger, frustration, impulsivity, anxiety, depression, schizophrenia
- May be direct result of damage to specific brain structures

Marijuana and PTSD

- O'Neil 2017, systematic review: 3 studies met inclusion criteria
- Two showed no relationship; one (with least risk of bias) was cohort study of veterans admitted in inpatient program for PTSD
- Use of marijuana was associated with worse symptoms and worse behaviour (including violence); stopping marijuana was associated with improvement
- Several clinical trials pending
- Preclinical studies: THC causes anxiety de novo; cannabidiol may have anxiolytic properties

Does marijuana help with post-ABI pain?

- Nampiaparampil 2008, systematic review of 20 studies: 57% of ABI patients reported chronic headache
- Can be severe, disabling, migraine-like
- Could find no clinical studies on effects of marijuana on ABI headache
- Best current guideline on cannabis for chronic pain:
- Preliminary guidance on authorizing dried cannabis for chronic pain and anxiety, College of Family Physicians of Canada 2014

Evidence for smoked cannabis and chronic pain

- 5 RCTs on smoked cannabis
- Total subjects = 180
- Duration range 3-15 days
- Subjects had severe neuropathic pain from MS or HIV or other causes
- The trials compared smoked cannabis to placebo, not to other treatments or to oral cannabis
- One trial that compared smoked cannabis to dronabinol
  - dronabinol had a longer duration of analgesia
  - Systematic review CFP Mailis 2016

Limitations of trials

- Outcomes only included subjective pain relief, not function
- Trials were small and lasted only a few days
- Cannot make conclusions about safety and efficacy in long term pain management
- Many subjects were experienced marijuana users
- Hard to distinguish pain relief from alteration of mood
- Much stronger evidence for effectiveness and safety of pharmaceutical cannabinoids

Adverse effects, safety

- Meta-analysis from 2009 (Sanchez et al), looked at 18 double-blind RCTS using pharmaceutical cannabinoids compared to placebo for chronic pain
- Alterations to perception OR 4.51
- Affect of motor function OR 3.93
- Altered cognitive function OR 4.46

Concerns with smoking

- Smoking: Very rapid rise and high peak in THC levels
- Causes intoxication, short duration of action
- Combustion creates many toxic products that are carcinogenic, atherogenic
- Products from licensed producers have very high THC % (20% or more)

Indications for cannabis

- Severe neuropathic pain, not responding to all other treatments including oral cannabinoids
- Not indicated for common pain syndromes seen in primary care, eg FM, MSK pain
  - No evidence of benefit
  - effective and safe alternatives

Contraindications

- Adolescents and young adults age 25 or less
- Patients with current, past, strong family history of psychosis
- Current substance use disorder
- Current or past cannabis use disorder
- Pregnant
- Current cardiovascular or respiratory illness

Precautions

- Past substance use disorder
- On higher doses of opioids or benzodiazepines
- Current anxiety or mood disorder
- Tobacco smoker
- High risk for cardiovascular disease

Precautions and contraindications in ABI

- Marijuana is contraindicated in many ABI patients:
- High prevalence of problematic substance use
- Current anxiety and mood disorders, psychosis

Dosing recommendations

- Titrate slowly
- Aim to improve function and relieve pain without causing cognitive impairment or intoxication
- Maximum dose 400-700 mg dried cannabis with THC concentration no more than 9% (with equal amounts of cannabidiol)

Management of requests for medical marijuana

- Do not prescribe if not indicated and/or contraindicated
- Explain to patients that evidence is lacking and adverse effects are serious
- Rule out cannabis use disorder (see later)
- Note: Reports of pain relief must be accompanied by evidence of improved function
- This is true for all analgesic medications
- Do not refer to medical marijuana clinics unless you are convinced they assess and prescribe based on evidence and best practices

Psychiatric and social harms of cannabis use

Self-reported problems among past 3 month users (15-24) (CAS 2004)

Problem (ASSIST)	
Strong desire to use	45.9%
Health, social, legal problems	8.9%
Failed expectations	12.2%
Friends concerned	27.3%
Failed control	54.0%

Prevalence of cannabis use disorder among youth

- Overall, an estimated 8% of recreational cannabis users meet DSM-IV criteria for dependence
- Prevalence might be higher in youth cannabis smokers
- In Ontario, the majority of patients seeking treatment for cannabis addiction are youth < 20, in high school (Urbanoski 2005)

Cannabis dependence in youth (2)

- Prospective study among 2500 cannabis-using youth (Nocon 2005):
  - Low frequency users: 22% reported 1 or more dependence criteria
    - Continued use despite consequences, withdrawal, loss of control, tolerance
  - High frequency users: 81% reported 1+ criteria
    - Co-occurring dependence on other drugs excluded

Withdrawal

- 44% of frequent users report clinically significant withdrawal symptoms
  - causing distress and relief smoking
- Two groups of symptoms:
  - 'weakness' (hypersomnia, weakness, psychomotor retardation)
  - anxiety, depression, insomnia, restlessness
- Onset days 1-3, peak 2-6, duration 4-14
  - Hasin 2008, Budney 2003

Cannabis and psychosis

- Case control, prospective studies confirm an association between cannabis use and later development of psychosis
- Meta-analysis: OR 2.0 (Moor 2007)
- Independent of confounding
- Early and frequent use may be greater risk (Hall 2006)
- Causation difficult to prove but is biologically plausible (dopamine hypothesis)

Cannabis and psychosis (2)

- Schizophrenics who are current cannabis users vs non-users:
  - less responsive to antipsychotics
  - higher risk of suicide
  - worse functioning
  - more hospitalizations
  - greater thought disturbance
- Abstinence with first episode psychosis improves global functioning, positive symptoms
  - Less effect with chronicity
- (Caspari 1999, Faridi 2012, Green 2005, Mullin 2012, Serafini 2011)

Anxiety and mood disorders

- Cannabis use associated with anxiety disorder in young adults (OR 2.5) Degenhardt 2012
- Evidence for link with depression is not as solid (Horwood 2012, Enrique-Garcia 2012)
- Eg Guttmanova 2017: prospective study of 808 subjects. Frequent use of marijuana in adolescence and young adulthood associated with generalized anxiety, cannabis use disorder, alcohol use disorder at age 33
- In preclinical studies, THC, especially at doses >5%, can induce fear, panic attacks de novo; whereas cannabidiol decreases anxiety

Cannabis and social harms in adolescents

- Cannabis use in adolescence associated with:
  - Harmful use of alcohol, tobacco and other drugs
  - Lower educational attainment
  - Criminal activity
  - Lower global IQ (current smokers, 5+/week)
  - Going on social assistance
- Harms are present even in occasional users, but increase with frequency of use
- Causal association not proven

Explanation for these associations

- Direct effects – chronic intoxication
  - cannabis acutely impairs memory, executive function
  - Long term impact not clear
- Indirect effects
  - peers who smoke cannabis are a negative influence
- Confounding factors
  - Adolescents with PTSD and anxiety disorders are more likely to smoke cannabis and do worse in school
  - Degenhardt 2010, Fergusson 2006, Fried 2002, Pedersen 2011, Cougle 2011

Cannabis use disorder

Clinical features

- Smokes daily, often large amounts (2+ grams)
- Spends a large amount of time smoking, neglecting other activities (school, work, family etc)
- Poor mood, poor psychosocial functioning
- Inability to reduce or abstain
- Presence of risk factors
  - ABI
  - Anxiety, mood, psychotic disorders
  - Current, past or strong family history of problematic substance use

Management

- Explain link between cannabis use and poor mood and function
- Explain that abstinence or reduced use will improve mood, function and pain
- Encourage attendance at addiction treatment
- HSC, CAMH
- Substance Use Services at SJHC, SMH, WCH
- Nabilone may be helpful - relieves withdrawal symptoms and cravings, is safe
- Other agents eg gabapentin may be helpful; more research needed