MARIJUANA AND KIDS: AN EVIDENCE-BASED EXAMINATION

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DISCLOSURES

• No financial disclosures
LEARNING OBJECTIVES

• Historical use of cannabis
• Review pharmacology of cannabis
• Discuss current evidence regarding use of marijuana
  • Medical therapy
  • Illicit use by children and adolescents

A HISTORY LESSON

• Cannabis used for medicinal reasons since 2000 BC
• US Pharmacopeia classified marijuana as a medical compound in 1851
  • Stayed on until 1942
• Criminalized in 1937
• Schedule I drug

LEGALIZATION FOR MEDICAL USE

• 23 states and DC have legalized marijuana
  • Range in 1 to 24 oz usable
  • 4 to 24 plants
• Recreational use
  • Washington, Colorado, DC
• 11 states likely to legalize in 2016
MONITORING THE FUTURE (2015) MARIJUANA USE

- Study of 8th graders in WA before and after legalization (Mason et al., 2015)
  - Increased use of marijuana
  - Lower alcohol and cigarette use, possibly substituting with marijuana
- Montana study of 17,482, age 13 to 19 yrs (Friese & Grube, 2013)
  - Increased lifetime and 30-day use
- Social norms and ease of access
- Monitoring the Future from 1991 to 2014 in states with medical marijuana laws (Hasin et al., 2015)
  - No increase with passing laws
  - Overall adolescent use higher in states with medical marijuana laws

MONITORING THE FUTURE (2015) VEY

LEGALIZATION AND ADOLESCENT USE

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CANNABINOIDS MEDICINES

- Cannabis-derived pharmaceuticals
  - Dronabinol (Marinol)
    - Schedule III
    - Contains THC
    - Label "pediatric dosage for chemo-associated emesis is same as adults"
  - Nabilone (Cesamet)
    - Schedule II
    - Contains THC
    - Label "safety and effectiveness not established...younger than 18 yrs"
  - Nabiximols (Sativex)
    - Cannabis-based oralmucosal spray
    - Approved in Canada, NZ and EU countries
    - Contains THC and cannabidiol (CBD)
    - UK Label "safety and effectiveness not established...younger than 18 yrs"

BOTANICALS

- "Medical" marijuana
  - Cannabis sativa
    - Uplifting and energetic
    - Best suited for day use
  - Cannabis indica
    - Relaxing and calming
    - Best suited for night use
  - Cannabis ruderalis
    - Low in THC
    - High in cannabidiol

PHARMACODYNAMICS

- Cannabinoids work on the cannabinoid receptors
  - CB1 found on basal ganglia (affecting motor activity), cerebellum (motor coordination), hippocampus (short-term memory), neocortex (thinking), and hypothalamus and limbic cortex (appetite and sedation)
  - CB2 found on immune cells and tissues, brain
CANNABIDIOL (CBD)

- The major non-psychotropic compound in cannabis
  - Low affinity for CB1 or CB2 receptors
  - Does not produce euphoria or intoxication
- Animal studies: anti-seizure, antioxidant, neuroprotective, anti-inflammatory, analgesic, anti-tumor, anti-psychotic, and anti-anxiety properties
- Epidiolex
  - a purified CBD extract

Volkow, 2015; Reddy & Golub, 2016

PHARMACOKINETICS

- Absorption
  - Rapidly absorbed from lungs
  - Lower bioavailability when taken orally
- THC 1/2 life for distribution is 0.5 hr and terminal 1/2 life is 30 hrs
- Cannabidiol terminal 1/2 life is 9 hrs
- Highly lipophilic
  - THC accumulates in the brain

DRUG-DOSE RELATIONSHIP

- Wide variation in reported doses to get desired effect
- Tolerance to THC
  - Downregulation of CB1 receptors and G-protein activation
  - Tolerance can develop in as few as 4 days
- Low dose: < 7 mg
- Medium dose: 7-18 mg
- High dose: > 18 mg
- Serum concentrations do not correlate with physiologic effect

Borgelt et al, 2013
DIFFERING RESPONSES TO CANNABIS

- LH, FSH, prolactin and growth hormone all decrease with long-term use
- Females with higher estrogen are more sensitive to effects of cannabis on pain, behavior and reward
- Patients with heart problems may have increased heart rate
  - Complicated by medications that also increase heart rate (amphetamines)
- Decreased alertness when used with benzodiazepines, opiates and TCAs

MEDICAL USE OF CANNABIS

- Nausea and vomiting from chemotherapy
- Appetite stimulation in HIV/AIDS
- Chronic pain
- Spasticity due to multiple sclerosis
- Gastrointestinal disorders
- Psychiatric disorders (depression/anxiety)
- HIV-associated sensory neuropathy
- Seizure disorder/epilepsy
- Parkinson disease
- Tourette Syndrome

Koppel et al, 2015; Whiting et al, 2015; Godsey & Grundmann, 2016

EVIDENCE IN CHILDREN: SEIZURES

- Marijuana-Derived Epilepsy Drug in Clinical Trial for Children with Uncontrolled Seizures
  - Multicenter (11 sites) trial
  - Epidiolex, a purified cannabinoid that comes in a liquid form containing no tetrahydrocannabinol (THC) for 12 weeks
  - 36.5% reductions in motor seizures (Devinsky et al, 2016)
EVIDENCE IN CHILDREN: SEIZURES

- Parent report studies
- Hussain et al (2015): online survey of parents who administer CBD oil to children with infantile spasms or Lennox-Gastaut
  - 85% reported reduction in seizures, 14% seizure free
- Press et al (2015): retrospective study of 75 pts with seizures on oral cannabis therapy (OCT) for seizures
  - 57% reported any improvement in sz, 33% reported >50% reduction in sz
  - 45.3% moved to Colorado for OCT

EVIDENCE IN CHILDREN: SPASTICITY

- Small study in Germany (N = 16, mean age 12.7 yrs)
- 2.5% oily tetrahydrocannabinol solution (dronabinol)
  - Dosage ranged from 0.08 to 1.0 mg/kg/day (mean 0.33 mg/kg/day)
  - Mean length of treatment 181 days
- Worked well to improve treatment-resistant spasticity
- Minimal side effects

Kuhlen et al, 2016

EVIDENCE IN CHILDREN

- Cancer treatment: no evidence found
- Ongoing studies
- ADHD: no evidence
- Tourette Syndrome: no evidence in children
ADVERSE EFFECTS: THE EVIDENCE

• Decreased cerebral blood flow in adolescents heavy users (Jacobus et al, 2012)
  • Normal after 4 weeks of abstinence
  • Structural and functional changes found in adolescents who use cannabis

ADOLESCENT USE AND PSYCHOSIS

• Increased incidence of psychosis in heavy cannabis users
• Longitudinal studies -> increased schizophrenia
  • 7. Self medicating
• Endocannabinoid system plays an important role in fundamental brain developmental processes
  • Use during adolescence can affect brain functions and behavior

Malone et al, 2010

ADVERSE EFFECTS IN STUDIES

• Devinsky et al (2016)
  • Somnolence 25%, decreased appetite 19%, diarrhea 19%, fatigue 13%, convulsion 11%, status epilepticus 6%
  • Increased seizures (13%) and somnolence/fatigue (12%)
  • Rare adverse events included developmental regression, abnormal movements, status epilepticus
EVIDENCE NEEDED!

- Prevalence of parents treating children with cannabinoids
- Tourette Syndrome in children and adolescents
- Spasticity in children
- Long term efficacy and adverse effects

QUESTIONS?

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REFERENCES


