Emerging Knowledge, Issues, and Challenges with Marijuana and Synthetic Cannabinoids

Activity Number: 0217-0000-16-131-L01-P, 1.50 hours of CPE credit; Activity Type: A Knowledge-Based Activity

Tuesday, October 25, 2016
10:15 a.m. to 11:45 a.m.
Diplomat Ballroom 3

Moderator: Marsha A. Raebel, Pharm. D., FCCP
Investigator, Pharmacotherapy Institute for Health Research, Kaiser Permanente Colorado Institute for Health, Denver, Colorado

Agenda

10:15 a.m. Emerging Knowledge About Marijuana and Synthetic Cannabinoids: Formulations, Pharmacodynamics, Medical and Recreational Use
  Bradley Carlson, Pharm. D.
  Former Chief Pharmacist and Vice President of Pharmacy Operations for LeafLine Labs, LLC, Minneapolis, Minnesota

11:00 a.m. Hazardous Use, Challenges, and Issues Associated with Legalization of Cannabis
  Laura M. Borgelt, Pharm. D., FCCP, BCPS
  Professor, University of Colorado Anschutz Medical Campus, Skaggs School of Pharmacy and Pharmaceutical Sciences and School of Medicine, Aurora, Colorado

Conflict of Interest Disclosures
Laura M. Borgelt: Clinical Investigator: (Colorado Department of Public Health and Environment), Grants: (Colorado Department of Public Health and Environment)
Bradley Carlson: Former Employee: (LeafLine Labs, LLC)
Marsha A. Raebel: no information provided

Learning Objectives
1. Describe the pharmacodynamics and pharmacokinetics of marijuana when used for medical and recreational purposes.
2. Compare and contrast common marijuana formulations and routes of administration.
3. Discuss the role of synthetic cannabinoids from the past to the future.
4. Discuss the pharmacology of endo- and exo-cannabinoids.
6. Outline use of cannabinoids for other conditions.
7. Discuss the effect of cannabis on the developing brain.
8. Review the adverse effects of marijuana.
9. Identify talking points for discussing medical and recreational marijuana use with a patient.
10. Discuss driving under the influence of cannabis.
11. Describe unanticipated consequences of legalizing marijuana.
Self-Assessment Questions

Self-assessment questions are available online at www.accp.com/am
Emerging Knowledge about Marijuana and Synthetic Cannabinoids: Formulations, Pharmacodynamics, Medical, and Recreational Use
Emerging Knowledge about Marijuana and Synthetic Cannabinoids: Formulations, Pharmacodynamics, Medical, and Recreational Use

Bradley D. Carlson, PharmD, RPh
Inpatient Clinical Pharmacist, Park Nicollet Methodist Hospital
St. Louis Park, MN
October 25th, 2016
precipice

noun prec·i·pice \ˈpre-s(ə-)pəs\  
: a very steep side of a mountain or cliff  
: a point where danger, trouble, or difficulty begins
THIS is why
I am HERE...
Where the magic happens

your comfort zone
Conflict of Interest

• Dr. Carlson is a former employee of LeafLine Labs, LLC (Minneapolis, MN)
• Dr. Carlson will be discussing unapproved drugs and uses
• Dr. Carlson has no relevant financial disclosures or other conflicts of interest influencing content of this presentation
Learning Objectives

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• Evaluate evidence for/against cannabis treatment for chronic cancer and non-cancer pain.
• Outline use of cannabinoids for other conditions.
BRIEF Cannabis History

• Plant has been valued for millennia!
• Used as medicine, textile, food
• Complex history of use and control of use
• Medical use and recreational use becoming more widely accepted in US (although being used medicinally in other countries for years)
The National Landscape

23 States + the District of Columbia have State-Based Medical Cannabis Programs

California was 1st State in 1996

Minnesota became the 22nd State in 2014

Additional 11 States Allow Limited Products

Four States Permit Recreational Use
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Medical Cannabis vs. Recreational Marijuana

• Recreational use titrates to a “high”
  • “Risk-Risk” utilization
• Medical use titrates to symptom relief
  • “Benefit - Risk” utilization
• PHARMACIST’S ROLE!!!!
• Some states allow different products / different quantities of product for medical vs. recreational
• PK / PD essentially the same; varies between patients and products
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Cannabis-Derived Pharmaceuticals

- Single molecule pharmaceuticals
  - Dronabinol (Schedule III)
  - Nabilone (Schedule II)
- Liquid extract: nabiximols (Sativex®)
  - Approved in 27 countries; U.S. - Phase III trials
- Liquid extract: cannabidiol (Epidiolex®)
  - FDA: orphan drug status for Dravet and Lennox-Gastaut syndromes
  - Expanded access INDs to several independent investigators

- Phytocannabinoid-dense botanicals
  - *Cannabis sativa* – medicinal plant (Schedule I)

*Slide used from Borgelt with permission.*
Single Molecule Pharmaceuticals

- Dronabinol (Marinol®) - synthetic THC
  - anorexia associated with weight loss in patients with AIDS
  - nausea and vomiting associated with cancer chemotherapy in patients who have failed to respond to conventional antiemetics
- Nabilone (Cesamet®) - synthetic THC similar
  - nausea and vomiting associated with cancer chemotherapy in patients who have failed to respond to conventional antiemetics
- Both agents have been utilized off-label for other indications
Whole Plant Extract Pharmaceuticals

Nabiximols (Sativex®)
* Spasticity (muscle stiffness/spasm) due to Multiple Sclerosis
* Neuropathic pain in MS
*** Adjunctive analgesic treatment in patients with advanced cancer who experience moderate to severe pain during the highest tolerated dose of strong opioid therapy for persistent background pain

Cannabidiol (Epidiolex®)
* Pediatric epilepsy
  - Lennox-Gastaut Syndrome
  - Dravet Syndrome
Synthetics: A Thing of the Past?

• Whole Plant Extracts = Entourage Effect?
Whole-Plant Extracts

- Cannabinoids
- Terpenes
- Lipids
- Flavonoids
- Sterols
- ENTOURAGE EFFECT!
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3 Most Common Routes of Administration

LUNGS
Vaporized or Smoked
Organic material, hash, waxes & extracted oils

ENTERAL
Oral Ingestion
Lipophilic, alcoholic, supercritical & subcritical oil extracts of plant material

TOPICAL
Application
Creams, buccal tinctures, and patches made from plant extracts
Inhalation Delivery of Cannabis

- Similar to IV bolus
- Passive diffusion into alveolar capillaries
- Bioavailability: 2-56%
- Fraction absorbed: 10-20%
- Rapid onset (sec-min)
- Maximal onset 30 minutes and lasting 2-3 hours
- Metabolism in liver, lung, and brain
- Elimination $t_{1/2} = 20$ hrs (2-13 days)
- Elimination primarily via feces (65%) and urine (20%)


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Enteral Delivery of Cannabis

- Variable absorption
- Bioavailability ranges 4-20%
- Onset: 30 minutes-2 hours
- Duration: 5-8 hours
- Metabolized primarily in the liver
  - 11-hydroxy-THC
- Elimination $t_{1/2} = 20-30$ hrs
- High inter- and intra-patient variability

References:
Pharmacotherapy 2013;33:195-209
Brit J Clin Pharm 2009;67(1):5-21
Clin Pharmacol Ther 1980 Sep;28(3):409-16

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Metabolism and Elimination

• Primary Hepatic via various CYP P450 Enzymes
  • THC = CYP2C9, CYP3A4
  • CBD = CYP2C19, CYP3A4

• Uridine diphosphate glucuronosyltransferases also play a role in metabolism

• In vitro Microsome studies suggesting many other elements involved in metabolism

• Other prescription medications influencing metabolism of Cannabis (and vice versa)
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The Human Endocannabinoid System

- Endocannabinoids and their receptors found throughout body: brain, organs, connective tissues, glands, and immune cells.
- In each tissue, the cannabinoid system performs different tasks; goal is always **homeostasis**
- When cannabinoid receptors are stimulated, a variety of physiologic processes occur
  - CB1 receptors: nervous system, connective tissues, gonads, glands, organs
  - CB2 receptors: immune system and associated structures
- Endocannabinoids are substances our bodies make naturally to stimulate CB1 and CB2
  - Anandamide
  - 2-arachidonoylglycerol (2-AG)

Slide used from Borgelt with permission.
Endocannabinoid Pharmacology

• Anandamide
  • partial agonist at CB receptors
  • slightly higher affinity for CB1
• 2-arachidonyl glycerol
  • full agonist at CB1 receptor
• Stimulation of CB receptors has an effect to suppress neurotransmission at both excitatory and inhibitory synapses
• Ultimate action of CB stimulation is preservation of homeostasis - varies greatly depending on organ/tissue
  • pain modulation, lipid metabolism, mood, motor function, appetite stimulation, GI function, CV function, etc.
The Human Endocannabinoid System: Targets for Cannabis Therapy
The “New Kid” on the Block...

The cannabinoid that has sparked the most interest is a non-psychoactive component called cannabidiol (CBD).


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Cannabis - Efficacy in Practice

• Few clinical trials exist
• Common phrase from practitioners:
  • “The jury is out” on efficacy
• Most evidence anecdotal
  • from personal experience, very positive!
• Many clinical trials used products that are not whole plant extracts
• Dronabinol and Nabiximols commonly utilized in clinical evaluations
Cannabis - Cancer-related Pain


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Minnesota Statistics

<table>
<thead>
<tr>
<th>Qualifying Condition</th>
<th>Patients: N (%)</th>
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<tbody>
<tr>
<td>Glaucoma</td>
<td>20 (1%)</td>
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<tr>
<td>HIV/AIDS</td>
<td>51 (3%)</td>
</tr>
<tr>
<td>Tourette Syndrome</td>
<td>29 (2%)</td>
</tr>
<tr>
<td>ALS</td>
<td>18 (1%)</td>
</tr>
<tr>
<td>Seizures</td>
<td>300 (20%)</td>
</tr>
<tr>
<td>Muscle Spasms</td>
<td>685 (45%)</td>
</tr>
<tr>
<td>Crohn’s Disease</td>
<td>106 (7%)</td>
</tr>
<tr>
<td>Cancer</td>
<td>392 (26%)</td>
</tr>
<tr>
<td>Terminal Illness</td>
<td>75 (5%)</td>
</tr>
</tbody>
</table>

Information from MDH, used with permission
Cannabis in Treatment of Pain

• In my personal experience:

• IT WORKS!!!!
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Widespread CB Receptors = Many Potential Targets for Therapy
Targets of Cannabis Therapies

**CB1 Receptors**
- Basal ganglia
  - Motor activity
- Cerebellum
  - Motor coordination
- Hippocampus
  - Short-term memory
- Neocortex
  - Thinking
- Hypothalamus & limbic
  - Appetite, sedation
- Pertaqueductal gray dorsol horn
  - Pain
- Immune cells

**CB2 Receptors**
- Immunologic cells
  - B lymphocytes
  - Natural killer cells
- Brain
  - Role not established

Slide used from Borgelt with permission.
Current Qualifying Indications in Minnesota

1. Cancer, with severe or chronic pain, or nausea/vomiting, or cachexia
2. Glaucoma
3. HIV/AIDS
4. Tourette’s Syndrome
5. Amyotrophic Lateral Sclerosis
6. Seizures, including those characteristic of epilepsy
7. Severe and persistent muscle spasms, including those characteristic of multiple sclerosis
8. Crohn’s Disease
9. Terminal Illness with life-expectancy < 1 year, with severe or chronic pain, or nausea/vomiting, or cachexia
10. Intractable Pain (added August 1, 2016)
Cannabis Research

- New dosage forms
  - Rectal, topical, transdermal, inhalation variations
- New indications
- Standardization of dosing
- Continued expansion of state programs
- Clinical trials?
Conclusions

• The PD/PK of Cannabis is similar between medical and recreational use; it varies between dosage forms and between patients

• Cannabis can be successfully utilized in a variety of different dosage forms, most commonly inhalation, oral and topical

• Synthetic cannabinoids have helped paved the way for medical use of cannabis; whole-plant extracts are the focus of many current medication producers

• Cannabis-derived medication works by regulating and supplementing the body’s endocannabinoid system

• Cannabis is being used successfully by patients with many disease states with many symptoms; more research needs to be done to expand and standardize these practices

• Pharmacists will have a key role to play as dosage forms and indications expand
Special Thanks

• Dr. Laura Borgelt
• Dr. Angela Birnbaum
• Joseph Friedman, RPh
• Dr. Brian Carlson
• Jon Lane
Combined Q & A Session following Dr. Borgelt’s Presentation
Thank you for your time and attention!

Bradley D. Carlson, PharmD, RPh
carl0887@umn.edu
Emerging Knowledge about Marijuana and Synthetic Cannabinoids: Formulations, Pharmacodynamics, Medical, and Recreational Use

Hazardous Use, Challenges, and Issues Associated with Legalization of Cannabis

Laura Borgelt, PharmD, FCCP, BCPS
University of Colorado Anschutz Medical Campus
Skaggs School of Pharmacy and Pharmaceutical Sciences
Aurora, CO
October 25, 2016
The Story...
Conflicts of Interest

Dr. Borgelt has no relevant financial disclosures.

Dr. Borgelt will be discussing unapproved drugs and uses.

Dr. Borgelt has served as a member of six working groups:

• Colorado Department of Public Health and Environment (CDPHE): Amendment 64 (Marijuana Legalization) Task Force Working Group: Consumer Safety and Social Issues

• State Licensing Authority Labeling, Packaging, Product Safety and Marketing

• State Licensing Authority Medical and Retail Marijuana Mandatory Testing and Random Sampling

• State Licensing Authority Serving Size and Product Potency

• CDPHE Retail Marijuana Public Health Advisory Committee

• CDPHE Pregnancy and Breastfeeding Guidelines Committee
Audience Question

I know someone who consumes marijuana for medical or recreational purposes.

1. Yes, medical purposes only
2. No, recreational purposes only
3. Yes, both
4. No
Audience Question

I believe the most common reason people seek out marijuana is to...

1. relieve pain
2. improve symptoms of nausea and vomiting
3. relieve muscle spasms associated with multiple sclerosis
4. get high
Learning Objectives

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Marijuana

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- Phytocannabinoid-dense botanicals
  - *Cannabis sativa* – medicinal plant (Schedule I)
Considerations for medical use of marijuana are different than considerations for recreational use of marijuana.

Medical use: benefit - risk

Recreational use: risk - risk
Targets of Marijuana

**CB1 Receptors**
- Basal ganglia
  - Motor activity
- Cerebellum
  - Motor coordination
- Hippocampus
  - Short-term memory
- Neocortex
  - Thinking
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Cannabis

- Plant-derived cannabinoids
  - $\Delta^9$-tetrahydrocannabinol - THC
  - $\Delta^8$-tetrahydrocannabinol - THC
  - Cannabidiol – CBD
  - Cannabinol - CBN
  - Cannabigerol - CBG
  - Cannabichromene - CBC
  - Cannabicyclol - CBL
  - Cannabielsoin - CBE
  - Cannabitriol - CBT
  - Miscellaneous
  - Cannabinodiol (air-oxidation)


https://medlineplus.gov/marijuana.html
THC Action in the Brain

Audience Question

At what age is the brain fully developed?

1. 15 years
2. 25 years
3. 35 years
4. No particular age – the brain is always developing
Retail marijuana public health information

Back to marijuana

Education and youth prevention resources for community agencies
Fact sheets, campaign information, effective prevention strategies, technical assistance requests, education program reports, trainings

Health care provider resources
Clinical guidance, patient fact sheets and resources

**Scientific literature review of marijuana-related health effects**
Summary and key findings, health topics, literature review process, future review of topics

Monitoring marijuana-related health effects
Summary and key findings, health effects data

Monitoring trends in marijuana use
Summary and key findings, monitoring changes in use patterns

Contact
Scientific Literature Review: Health Topics

- Marijuana use during pregnancy and breastfeeding
- Unintentional marijuana exposures in children
- Marijuana use among adolescents and young adults
- Marijuana dose and drug interactions
- Marijuana use and neurological, cognitive and mental health effects
- Marijuana use and respiratory effects
- Marijuana use and extrapulmonary effects
- Marijuana use and injury

https://www.colorado.gov/cdphe/scientific-literature-review-marijuana-related-health-effects
### Evidence of Marijuana Effects on Adolescents and Young Adults

<table>
<thead>
<tr>
<th>Substantial</th>
<th>Moderate</th>
<th>Limited</th>
<th>Insufficient</th>
<th>Mixed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less high school graduation</td>
<td>Impaired cognitive abilities and academic performance after 28 days abstinence</td>
<td>Less likely to earn college degree</td>
<td>Lower IQ after brief abstinence</td>
<td>Lower future IQ scores</td>
</tr>
<tr>
<td>Can develop marijuana addiction‡</td>
<td>Increased MJ use and addiction‡ after adolescence</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment for MJ addiction can reduce MJ use and dependence</td>
<td>Quitting MJ lowers risk of cognitive and mental health effects</td>
<td></td>
<td></td>
<td>Suicidal thoughts or attempts</td>
</tr>
<tr>
<td>Other illicit drug use and addiction‡ after adolescence</td>
<td>Alcohol or tobacco use and addiction‡ after adolescence</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psychotic symptoms in adulthood</td>
<td>Psychotic disorder in adulthood (heavy users)</td>
<td></td>
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</tr>
</tbody>
</table>

THC Action in the Developing Brain

Endocannabinoid System

Learning Objectives

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• Discuss driving under the influence of cannabis.
• Describe unanticipated consequences of legalizing marijuana.
Potential Physiologic Responses to Cannabis

- Improves sleep
- Anti-seizure effects and neuroprotection
- Reduces anxiety and psychotic symptoms/PTSD
- Prevents nausea and stimulates appetite
- Reduces intraocular pressure
- Bronchodilator
- Relaxes muscles and reduces muscle spasms
- Relieves pain (especially neuropathic)
- Anti-inflammatory
- Anti-proliferative
- Anti-viral

With potential adverse effects.

Which of the following is/are common adverse effects of marijuana?

1. Headache
2. Slowed reaction time
3. Decreased heart rate
4. Insomnia
5. All of the above
Marijuana Adverse Effects

- Cardiovascular
- Respiratory

EUPHORIA

Nervous System

- Tachycardia
- Palpitations
- Hypertension

- Coughing
- Wheezing
- Sputum production

- Lethargy, Sedation, Slowed Reaction Time, Visual Disturbances
- Psychological dysfunction: impaired coordination, memory formation, recollection, focus

Adverse Effects of Marijuana

**Effects of Short-term Use**
- Impaired short-term memory
- Impaired motor coordination
- Altered judgment
- Motor vehicle accidents (2x)
- Paranoia and psychosis (high doses)

**Effects of Long-term/Heavy Use**
- Addiction (9% overall)
- Altered brain development*
- Cognitive impairment (with lower IQ)*
- Diminished life satisfaction and achievement*
- Poor educational outcome
- Symptoms of chronic bronchitis
- Increased risk of chronic psychosis disorders

*Effect is strongly associated with initial marijuana use early in adolescence

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Patient Case

• 2 yo male with lethargy is brought to the emergency department of Children’s Hospital Colorado. Several tests are performed including:
  • Urinalysis
  • Comprehensive metabolic panel
  • Complete blood count
  • APAP/ASA levels
  • EKG
  • Urine toxicology
  • CT head
  • Chest X-ray

What are potential causes of his lethargy?
Should he be admitted?

Patient Case, con’t

- Admitted to hospital
- Unintentional exposure to marijuana
- Source of marijuana: babysitter

What counseling should occur for this patient and/or family?

Patient Case

• 17 yo male displays unusual behavior in the classroom and is brought to the counselor’s office
• Counselor verifies that the student is high and obtained cannabis (gummy bears) from a friend
• Student admits to using cannabis several times per week; claims it reduces his anxiety and anger
• Student does not think it impacts his school grades or ability to play sports (football and basketball)

What counseling should occur for this student?
Patient Case

• 27 yo female comes to clinic for second trimester prenatal visit (24 weeks pregnant)
• Medications: prenatal vitamin once daily
• Social history: no alcohol, no tobacco, smokes cannabis one to two times daily
  • Initially started cannabis to relieve nausea in first trimester; continued cannabis because it “improved sleep”
• She has heard about cannabis having potential harm on the fetus, but does not think the studies were done well enough to make conclusions about harm; feels benefits outweighs any risks

What counseling should occur for this patient?
Patient Case

- 62 yo female with long-standing diabetes and severe neuropathic pain; other conditions include hypertension, dyslipidemia, and arthritis

- For neuropathic pain and arthritis, she has tried seven different FDA-approved or OTC medications; currently taking APAP, oxycodone and pregabalin

- Started cannabis about 3 months ago
  - Vaporizes THC:CBD (1:1) twice daily

- Reduced oxycodone dose by 30% since cannabis; has continued APAP, pregabalin and cannabis

What counseling should occur for this patient?
Counseling strategies vary based on individual patient situations. Efforts should be made to determine medical history, medication history, social history, and other patient-specific factors to determine what, why, and how cannabis is being used.

*Pharmacists: also screen for drug interactions*
Counseling Strategies: Medical Cannabis

• Reason for use
  • “Patients use cannabis for many different conditions. For what condition(s) are you using cannabis?”

• Cannabis use (formulation, dose, frequency)
  • “By what method(s) do you use cannabis?”
  • “What strain and/or cannabinoid concentrations are you using?”
  • “How often are you using cannabis?”

• Concurrent drug use
  • “What other medications are you taking at this time?”

• Screen for drug interactions

## Drug Interactions

<table>
<thead>
<tr>
<th>Cannabinoid</th>
<th>CYP-450 2C9</th>
<th>CYP-450 2C19</th>
<th>CYP-450 3A4</th>
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<tbody>
<tr>
<td>Δ9-THC</td>
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<tr>
<td>Δ8-THC</td>
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</tr>
<tr>
<td>CBD</td>
<td></td>
<td>*</td>
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<tr>
<td>CBN</td>
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</table>

Drug Metab Rev. 2014;46(1):86–95

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Clinically Important Drug-Drug Interactions

- Chlorpromazine
- Clozapine
- CNS depressants
- Disulfiram
- Hexobarbital
- Hydrocortisone
- MAO inhibitors
- Phenytoin
- Theophylline
- Warfarin

*Note: significant synergistic interaction found between CBD and levetiracetam. Significant antagonistic interactions noted with CBD + clobazam and CBD + carbamazepine. (AES Annual Meeting December 2015)

https://www.colorado.gov/pacific/cdphe/retail-marijuana-public-health-advisory-committee
Accessed 12/23/15
http://www.medicalnewstoday.com/articles/303725.php
Accessed 12/23/15
Counseling Strategies: Medical Cannabis

• What to expect
  • “What benefits did your provider tell you to expect by using cannabis?”
  • “What adverse effects did your provider tell you to expect?”

• When to seek further medical attention
  • Bothersome psychoactive effects
  • Cannabinoid hyperemesis syndrome (cyclic vomiting)
  • Withdrawal symptoms (if discontinuing)

• Follow-up when needed
  • Contact pharmacist or prescriber if any adverse effect becomes too bothersome or if any questions about marijuana use

Role Play
How to Talk to Youth about Marijuana

http://goodtoknowcolorado.com/youth-prevention/talking-to-youth

http://goodtoknowcolorado.com/content/resources/Good-to-Know-Colorado_Youth-Prevention_Infographics.pdf
Presenter Recommendations

1. Ask about the use of marijuana and consider screening in high-risk patients
2. Educate women about impact of cannabis during pregnancy and lactation
3. Strongly advise discontinuation or use harm-reduction
4. Offer drug services/counseling and/or cognitive behavioral therapy
5. Perform appropriate developmental milestones
6. Counsel about patient safety issues including keeping out of the reach of children and using proper packaging and labeling of marijuana
7. Avoid second hand/passive exposure
8. Review hospital policies and procedures
Learning Objectives

• Discuss the effect of cannabis on the developing brain.
• Review the adverse effects of marijuana.
• Identify talking points for discussing medical and recreational marijuana use with a patient.
• **Discuss driving under the influence of cannabis.**
• Describe unanticipated consequences of legalizing marijuana.
Colorado saying:

“People who are drunk go through red lights.
People who are high stop at green lights.”
# Marijuana Use and Injury

<table>
<thead>
<tr>
<th>Substantial</th>
<th>Moderate</th>
<th>Limited</th>
<th>Insufficient</th>
<th>Mixed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased MV crash risk (approximately double)</td>
<td>Increased risk of workplace injury</td>
<td>Injury risk differs by use frequency for MV crash</td>
<td>Increased risk of non-traffic injury</td>
<td></td>
</tr>
<tr>
<td>THC level and MV crash risk</td>
<td></td>
<td></td>
<td>Combined use and non-traffic injury</td>
<td></td>
</tr>
<tr>
<td>Combined use with alcohol increases MV crash risk</td>
<td></td>
<td></td>
<td>Increased risk of recreational injury</td>
<td></td>
</tr>
</tbody>
</table>

Patient Case

A man in a MVA is found to have a blood THC concentration of 10 ng/ml. House Bill 1325 set THC limit at 5 ng/ml. Which of the following is true?

1. The man did not reach the level of impairment
2. The man was above the known level of impairment
3. The level of presumptive impairment is not known
4. It is not known if the man was impaired with this concentration
Learning Objectives

• Discuss the effect of cannabis on the developing brain.
• Review the adverse effects of marijuana.
• Identify talking points for discussing medical and recreational marijuana use with a patient.
• Discuss driving under the influence of cannabis.
• Describe unanticipated consequences of legalizing marijuana.
Unanticipated Consequences: Health Topics

- Marijuana use during pregnancy and breastfeeding
- Unintentional marijuana exposures in children
- Marijuana use among adolescents and young adults
- Marijuana dose and drug interactions
- Marijuana use and neurological, cognitive and mental health effects
- Marijuana use and respiratory effects
- Marijuana use and extrapulmonary effects
- Marijuana use and injury

Patient Safety Issues

• Consistency (or lack thereof)
  • Quality and purity
• Packaging
• Labeling
• Testing – content and contaminants
• Accuracy of education provided

Medical Cannabis and Opioid Use
States with medical cannabis laws had a 24.8% lower mean annual opioid overdose mortality rate (95% CI, –37.5% to –9.5%; P = .003) compared with states without medical cannabis laws.

This association strengthened over time:
- Year 1 (–19.9%; 95% CI, –30.6% to –7.7%; P = .002)
- Year 2 (–25.2%; 95% CI, –40.6% to –5.9%; P = .01)
- Year 3 (–23.6%; 95% CI, –41.1% to –1.0%; P = .04)
- Year 4 (–20.2%; 95% CI, –33.6% to –4.0%; P = .02)
- Year 5 (–33.7%; 95% CI, –50.9% to –10.4%; P = .008)
- Year 6 (–33.3%; 95% CI, –44.7% to –19.6%; P < .001)

Medical Cannabis and Opioid Use

• 244 medical cannabis patients with chronic pain in Michigan

• Survey of 46 questions
  • Medical condition(s) for which cannabis was used
  • Method/frequency of cannabis use
  • Changes in noncannabis medication use
  • Changes in medication side effects
  • Quality of life changes since starting cannabis use
  • Demographic information
  • 2011 Fibromyalgia Survey Criteria (0-31 score)

<table>
<thead>
<tr>
<th>OUTCOME OF INTEREST</th>
<th>PATIENT RESPONSES (n=244) Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibromyalgia score (0-31)</td>
<td>9.23 (5.52)</td>
</tr>
<tr>
<td>Opioid use change</td>
<td>−63% (46%)</td>
</tr>
<tr>
<td>Degree to which side effects of medication affect daily function (before using medical cannabis); scale from 1 to 10</td>
<td>6.44 (2.91)</td>
</tr>
<tr>
<td>Degree to which side effects of medication affect daily function (after using medical cannabis); scale from 1 to 10</td>
<td>2.77 (2.35)</td>
</tr>
<tr>
<td>Number of medication classes used (before cannabis use)</td>
<td>2.35 (1.43)</td>
</tr>
<tr>
<td>Number of medication classes used (after cannabis use)</td>
<td>1.82 (.94)</td>
</tr>
<tr>
<td>Quality of life change</td>
<td>45% (28%)</td>
</tr>
</tbody>
</table>
Conclusions

• Cannabis has potential negative impact on the developing brain.

• Adverse effects of cannabis affect the cardiovascular, respiratory, and nervous systems.

• Discussing medical and recreational marijuana use with patients should be individualized and include screening for drug interactions.

• Use of cannabis is associated with increased risk of motor vehicle crashes and crash risk is associated with THC level.

• Several unanticipated consequences of legalizing marijuana exist including patient safety and public health concerns.
QUESTIONS?
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