Caroline DeVincenzi, DMD, & Barry Taylor, DMD, FAGD, FACD, CDE

Course 8107: “Green Dentistry: THC and Teeth? What you Need to Know About Cannabis”

Thursday, April 6
9 am - 12 pm
Green Dentistry: THC and Teeth? What you Need to Know About Cannabis

Caroline DeVincenzi, DMD
Barry Taylor, DMD, FAGD, FACD, CDE
Thursday April 6, 2017
Course Objectives

• Understand the pharmacology and pharmacokinetics of marijuana

• Understand interactions of THC with commonly used prescribed medications and be familiar with medical emergencies related to THC

• Understand how marijuana usage by patients effects their oral health; specific focus on oral pathology, caries risk, and periodontal disease

• Learn how to communicate with your patients regularly using cannabis

• Explore future areas of research in regards to periodontal health, wound healing, and caries control
Current Marijuana Outlook in the United States

- There are 8 states with recreational marijuana available and roughly 22 million individuals using cannabis monthly.
The Endocannabinoid System

• Central and peripheral modulation via CB1 and CB2 G-protein coupled receptors

• Therapeutic potential for treating epilepsy, nausea, Multiple Sclerosis, cancer, pain, inflammation, obesity, Parkinson’s Disease, Rheumatoid Arthritis, etc.

The Cannabinoid Ligands

- **The Endocannabinoids**
  - Endogenous ligands
  - Anandamide and 2AG

- **The Phytocannabinoids**
  - Plant derived ligands
  - THC, CBD and many more

- **The Synthetic Cannabinoids**
  - Chemically derived
  - Nablione, Dronabinol and more
The Cannabinoid Receptors

- **The CB1 Receptor**
- **The CB2 Receptor**

Both receptor types can control central and peripheral functions, including:

- Neuronal development, transmission and inflammation
- Cardiovascular function
- Respiratory function
- Reproductive function
- Hormone release and action
- Bone formation
- Energy metabolism
- Cellular functions - i.e. cell architecture, proliferation, motility, adhesion and apoptosis

Routes of Administration

- **Inhalation**
  - Smoking
    - “Joint” = a marijuana cigarette
  - Pipe
    - “Bong” = a marijuana water pipe
- **Vaping**
  - Using herbs, butane hash oils (BHOs = “dabs”) or e-liquid
- **Oral**
  - “Edibles”
- **Topical**
  - Lotion, chapstick
Bioavailability

• Inhalation - THC bioavailability averages 30%

• Oral - THC bioavailability averages only 4% to 12% due to the first pass effect
  
  • Absorption is highly variable

• Inhalation and oral administration both allow for formation of an active metabolite — 11-hydroxy-THC (11-hydroxy-delta 9-tetrahydrocannabinol)

  • 20% of inhaled THC becomes 11-hydroxy-THC versus 100% 11-hydroxy-THC formation from oral dosing

Distribution

“...thresholds for blood levels of THC do not provide a consistent index of behavioral impairment across individuals with different patterns of THC exposure.”


Onset and Duration

- **Inhalation:**
  - Onset: 0-30 minutes
  - Duration: +/- 2 hours

- **Oral:**
  - Onset: 30-120 minutes
  - Duration: 6-8 hours


***THC-COOH = 11-nor-9-carboxy-delta 9-tetrahydrocannabinol = an inactive metabolite***
Mechanism of Action


Table 1. Examples of the association between endocannabinoid receptor location, probable physiologic function, and the potential effects of marijuana.

<table>
<thead>
<tr>
<th>Normal Endocannabinoid Receptor Location</th>
<th>Endocannabinoid regulation of normal physiologic function</th>
<th>Potential effects of marijuana</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebral cortex, hippocampus, limbic system</td>
<td>Judgment, cognition, memory, alertness, mood and behavior, perception of time/color/sound</td>
<td>Impaired judgment, cognition, memory, alertness, changes in mood and behavior, altered or distorted perception of time/color/sound</td>
</tr>
<tr>
<td>Basal ganglia, cerebellum</td>
<td>Coordination, movement</td>
<td>Incoordination</td>
</tr>
<tr>
<td>Hypothalamus</td>
<td>Appetite</td>
<td>Increase in appetite</td>
</tr>
<tr>
<td>Medulla</td>
<td>Nausea and vomiting</td>
<td>Reduction in nausea/vomiting</td>
</tr>
<tr>
<td>Dorsal afferent spinal cord and peripheral nociceptors</td>
<td>Pain perception</td>
<td>Reduction in pain perception</td>
</tr>
<tr>
<td>Visual system</td>
<td>Intraocular pressure</td>
<td>Intraocular pressure reduction</td>
</tr>
<tr>
<td>Cardiovascular system</td>
<td>Heart rate, blood pressure</td>
<td>Acute increase in heart rate and supine or sitting blood pressure</td>
</tr>
<tr>
<td>Gastrointestinal system</td>
<td>Motility</td>
<td>Reduction in motility</td>
</tr>
<tr>
<td>Immune system</td>
<td>Immunity</td>
<td>Variable stimulation and/or suppression</td>
</tr>
</tbody>
</table>

Metabolism and Elimination

- THC is metabolized in the liver by cytochrome p450 enzymes
  - CYP2C9 and CYP3A4
  - Biotransformation of THC to active metabolite 11-hydroxy-THC
- Excretion via feces and urine
- Cannabinoids are highly lipophilic, therefore body fat provides long term storage of cannabis metabolites
  - Tissue elimination in 7 days
  - Total elimination after 30 days
## Drug Interactions

<table>
<thead>
<tr>
<th>Inhibitors of CYP2C9:</th>
<th>Inhibitors of CYP3A4:</th>
<th>Caution with CNS depressants/sedative agents:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amiodarone</td>
<td>Ketoconazole</td>
<td>Opioids</td>
</tr>
<tr>
<td>Cimetidine</td>
<td>Clarithromycin</td>
<td>Alcohol</td>
</tr>
<tr>
<td>Cotrimoxazole</td>
<td>Erythromycin</td>
<td>Benzodiazepines</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>cyclosporine</td>
<td>Ketamine</td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>Verapamil</td>
<td>Propofol</td>
</tr>
<tr>
<td>Fluvoxamine</td>
<td>Itraconazole</td>
<td></td>
</tr>
<tr>
<td>Fluconazole</td>
<td>Boceprevir</td>
<td></td>
</tr>
<tr>
<td>Voriconazole</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Acute Health Effects of Marijuana Use

- Within a few minutes:
  - Heart rate (HR) and blood pressure (BP) increase
    - 20-50 bpm change in HR
  - **Risk of myocardial infarction (MI) - heart attack - is nearly 5 times baseline risk within the first hour of smoking**
  - Bronchodilation
  - Vasodilation of vessels in the eye — bloodshot eyes
  - **Orthostatic hypotension** — head rush or dizziness when standing upright, fainting or falling
  - Impaired short-term memory
  - **Impaired attention, judgment, and other cognitive functions**
  - Impaired coordination and balance
  - Anxiety and paranoia
  - Psychosis (uncommon)

Chronic Health Effects of Marijuana Use

- Increased risk for chronic cough, bronchitis — airway inflammation
- Increased airway resistance
- Lung hyperinflation

- Decreased respiratory immune function
  - Increased risk of respiratory infections — i.e. pneumonia

- Potential for marijuana addiction
  - Cannabis use disorder or cannabis dependence defined in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5)
  - Increased risk of other drug and alcohol use disorders

- Increased risk of non-seminomatous testicular germ cell tumor
  - Aggressive form of testicular cancer affecting young adult males

- Increased risk of schizophrenia in people with genetic vulnerability
  - Often reported co-occurring symptoms/disorders with chronic marijuana use
  - Research has not determined whether marijuana is causing these mental problems, or simply associated with them

- Impairments in learning and memory with potential loss of IQ
  - Among individuals with persistent marijuana use disorder who began using heavily during adolescence

Marijuana and Oral Pathology

Table 3 A summary of the oral implications of cannabis use

<table>
<thead>
<tr>
<th>Oral implications of cannabis use</th>
<th>Associated implications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dry mouth (Xerostomia) - short term</td>
<td>Increased risk of caries. Increased risk of periodontal disease. Increased risk of frictional injuries. Halitosis.</td>
</tr>
<tr>
<td>Thermal injury</td>
<td>Hyperkeratinisation due to higher combustion temperature of cannabis.</td>
</tr>
<tr>
<td>Leukoedema</td>
<td>Normal variation. Clinically detectable due to multifactorial reasons: genetics, alcohol, tobacco and cannabis use.</td>
</tr>
<tr>
<td>Candidal infection</td>
<td>Increased risk of candidal infection – poor oral hygiene/denture hygiene – nutritional deficiency.</td>
</tr>
<tr>
<td>Oral cancer</td>
<td>Cannabis contains similar carcinogens to tobacco. Possibility of a link with cannabis use. However more evidence required.</td>
</tr>
</tbody>
</table>

- Head and neck cancers: +/-
- Lung cancer: —
- Testicular cancer: +

“For other cancer sites, there is still insufficient data to make any conclusions. Considering that marijuana use may change due to legalization, well-designed studies on marijuana use and cancer are warranted.”


Marijuana and Periodontal Disease

- Periodontal disease progression accelerates with age, especially among tobacco and cannabis smokers

- Marijuana use over 20 years is associated with periodontal disease

- Cannabis use is associated with deeper probing depths, more clinical attachment loss, and higher odds of having severe periodontitis
Marijuana and Dental Caries

- Schulz Katterbach MS. Cannabis and caries does regular cannabis use increase the risk of caries in cigarette smokers? Zurick Open Repos Arch 2009;119:576-583
  - 85 participants
  - 63% consumed "sweet" foods and drinks post use
  - 6x as many decayed surfaces
  - 198 young adult participants, also used amphetamines
  - Decrease in parotid saliva flow rate
  - pH dropped from 7.5 to 6.9
Managing Marijuana-Using Patients

- Questions to ask:
  - What type of marijuana do you use?
    - Do you know the THC/CBD concentration?
    - Do you know the name of the strain of cannabis you’re using?
  - How do you use it?
    - i.e. smoking vs. vaping vs. oral
  - How often do you use it?
  - How long have you been using it?
  - Why are you using it?

- Borrowing from Tobacco Cessation protocol:
  - Ask
  - Advise
  - Assess
  - Assist
  - Arrange
Marijuana Smokers vs. Tobacco Smokers

Figure 19. Daily Cigarette Use among Past Month Cigarette Smokers Aged 12 or Older and Smoking of One or More Packs of Cigarettes per Day among Current Daily Smokers: Percentages, 2014

22 million individuals using cannabis monthly and 22 million “less than daily” tobacco smokers

Reverse gateway theory:
Cannabis use will lead to the use of other “safer” substances, like nicotine and alcohol

Table 2 The difference between tobacco and cannabis

<table>
<thead>
<tr>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cannabis joints are usually smoked for a longer period of time than tobacco.</td>
</tr>
<tr>
<td>Cannabis joints are usually smoked to a shorter joint length, which results in a greater number of toxins entering the mouth.</td>
</tr>
<tr>
<td>Cannabis has a higher combustion temperature compared to tobacco.</td>
</tr>
<tr>
<td>There is greater carboxyhaemoglobin concentration and tar retention in lower airway in cannabis smokers.</td>
</tr>
<tr>
<td>Tobacco found in cigarettes is regulated. Whereas, cannabis is a non-regulated substance.</td>
</tr>
<tr>
<td>Tobacco is usually smoked more frequently than cannabis due to the shorter half life of nicotine.</td>
</tr>
</tbody>
</table>

Substance Abuse and Mental Health Services Administration = SAMSA


Retrieved from http://www.samhsa.gov/data/

“Cannavaping”

- **Health effects are largely unknown**, but vaping cannabis is marketed as the safer alternative to other inhalation methods.

- Risk of appealing to children and teenagers.

- Potential for increased use frequency, leading to increased addiction risk.

- Increased environmental and second-hand exposure due to **discrete use** in many public places.

- Increased vaping could dissociate cannabis and tobacco.
  
  - Therefore, reduce the risk of cannabis users becoming tobacco users.

Future Investigations

• Does cannabis smoking increase the risk for lung cancer?
• Is cannabis use a risk factor for periodontal disease?
• Is cannabis use a risk factor for dental caries?
• Does cannabis use lead to oral and/or head and neck cancers?
• Is cannabis vaping a viable alternative to cannabis smoking?
• Do cannabinoids provide any therapeutic benefit for dentists?
  • Pain modulation
  • Inflammation
QUIZ

1. What are the two main constituents of cannabis?
2. What class of drugs should be used with the most caution when prescribing for a cannabis-using patient?
3. Which acute reactions after cannabis use are likely to cause a medical emergency in your office?
4. Which type of oral lesions might you expect to see with a cannabis-using patient?
5. Is your cannabis smoking patient at a higher risk for periodontal disease than a non-smoking patient?
6. Is your cannabis smoking patient at a higher risk for cancer than a non-smoking patient? Which cancer type?
7. Is marijuana addictive?
8. Does your cannabis smoking patient automatically have a high caries risk?
9. Is acute cannabis use a contraindication for routine dental care?
10. Should you incorporate cannabis cessation protocols in your office?
1. THC + CBD
2. CNS depressants
3. Tachycardia (potentially inducing an acute MI) + orthostatic hypotension
4. Leukoedema, hyperkeratosis and candidiasis
5. Yes - it appears so, sigh…
6. Yes - testicular cancer, maybe H+N cancer…TBD
7. Yes - it can be
8. Maybe - still note your patient’s specific risk/protective factors and individualize your patient’s care
9. Up to you - there are no current national/state guidelines
10. Also, up to you - but hopefully you now have the information to engage your patients appropriately and provide them with the limited information you have