Cannabis & Cannabinoids for Pain Management:

What Nurses Need to Know!

Brenda Nordstrom, DNP, BS, RN, PMGT-BC, CHPN

MI NURSES Association
Hi my name is Dr. Brenda Nordstrom, and this presentation is on the relationship between adverse childhood experiences other traumas in pain management.

I have a bit of an eclectic nursing background and I am currently teaching nursing while also working as a relief nurse in home hospice. However, what peaked my interest in connecting trauma with pain management was my work with human trafficking survivors. I am a strong advocate for trafficked persons and volunteer for a local service provider and I am a healthcare trainer for my regional human trafficking task force. The more I interacted with not only human trafficking survivors but others who have experienced adverse childhood experiences and other trauma, I realized that nurses needed to learn about and understand the link between the mental and physical aspects of the pain experience.

When I first ventured into providing education about trauma and pain it was specifically for hospice nurses. However, I think the information is very applicable for all nursing specialties.
Outcomes:

01 Examine the history and legality of cannabis use

02 Recognize the importance of the endocannabinoid system in pain management

03 Explore cannabis & cannabinoid pharmacology with accompanying nursing considerations
History & Legality

1. Early History
2. 20th Century
3. Current Laws
The cannabis plant is native to Central Asia since prehistoric times, and it quickly became well-known as it traveled west. It originated in the Kush Himalayan foothills then migrated across the globe, primarily due to the herb’s role as a fiber and psychoactive flower. Neolithic people had many uses for the cannabis plant during ancient times. It provided fiber for textiles, and it was a food source. It also quickly became a part of medicinal concoctions as part of ritual preparations. It is hypothesized that people began smoking cannabis around the 5th century B.C. as part of burial ceremonies.

In 1993, a very fascinating find was made in the mountains of Russia—a well-preserved mummy who was known as the “Siberian Ice Princess”. She was a 2,500-year-old mummy who was buried with cannabis. Scientists’ examination revealed that she suffered from metastatic breast cancer and other ailments. They believed she was medicating with cannabis and therefore it was buried with her.

As China was the epicenter of hemp cultivation—both textile and medicinal varieties—it is no wonder that written evidence demonstrates that the Chinese people used cannabis for medicinal purposes more than 1,800 years ago. They even developed a unique specialty called Achene (a-ken) that utilized the seeds of the cannabis flower. Cannabis seeds were also consumed as food during ancient Chinese times.
Early History

- Shen-Nung (2,700 BC) – emperor and medicine man
  - More than 100 ailments
  - Pain, malaria, mental illness, cough, seizures, insomnia
- Hua T’O (approx. 117-207 AD) – founder of Chinese surgery
  - “Ma-yo” = boiled hemp compound, mixed with wine
  - Abdominal & other surgeries
Eventually, the cannabis plant migrated around the globe. Starting with India, then to the Middle East, Central Asia, Africa, Europe, & then ultimately finding its way to the Americas.
Early History --> 1800s

- Colonial-era settlers required to grow hemp
- 1600s – Virginia Assembly law
- Hemp & cannabis used for sailing
  - Rigging, sails, rope, & textiles

Medicinal cannabis developed reputation as curative
19th – 20th Century

Dr. William B. O’Shaughnessy

- Researched cannabinoid therapy
  - Animal testing – validated safety
- First to note biphasic effects
- Rabies, cholera, tetanus, epilepsy, rheumatism
- Well-documented literature
  - “On the preparations of the Indian hemp, or gunjah”
Dr. J. R. Reynolds

- Physician to Queen Victoria of England
- Cannabis for menstrual cramps & sleep
- Published in *The Lancet*
  - “Therapeutic uses and toxic effects of Cannabis Indica”
- Prescribed cannabis >30 years
  - Insomnia, dysmenorrhea, neuralgia, tics, & spasms
- Advised “start low, go slow”
19th – 20th Century

• More than 100 research articles
• 1854 – declared by U.S. Pharmacopoeia a “wonder drug”
• 1860 – Ohio State Medical Society research
  • Migraines, cough, inflammation, bronchitis, postpartum depression
  • Medicinal usage grew rapidly until early 1900s
• No stigma attached
• Available for purchase through Sears
20th Century Prohibition

• Unable to harvest consistent standardized product
• Pharmacies unable to synthesize
• Pure Food and Drug Act of 1906
  • Banned sale of “impure or falsely labeled food or drugs”
    • Truth in advertising
    • Labeled an intoxicant & government regulated
    • Alcohol, opiates, cocaine, chloral hydrate, cannabis

Pg 11-12
Required listing all ingredients on the label – cocaine in coca cola
20th Century Prohibition

- Harrison Narcotics Tax Act of 1914
  - Held physicians accountable
  - Doctors were arrested, licenses revoked
    - Jail time – prevent prescribing opiates (cannabis)
- Late 1920s – Narcotic Farms Act
  - Misclassified “Indian Hemp” as a habit forming narcotic
20th Century Prohibition

• 1930s – Federal Bureau of Narcotics (FBN)
  • Harry J. Anslinger – director, alcohol prohibitionist enforcer
  • Late 1930s cannabis prohibition replaced alcohol

"MARIJUANA IS THE MOST VIOLENCE-CAUSING DRUG IN THE HISTORY OF MANKIND."
- HARRY J. ANSLINGER -
20th Century Prohibition

- AMA endorsed medical cannabis use
- However
- Marijuana Tax Act of 1937 to 1969
  - Allowed physicians to prescribe
  - Decreased demand for medicinal use
  - Prevalent recreational use by BIPOC
- FBN & Mr. Anslinger heavily regulated
  - Physicians eventually stopped prescribing
- 1941 – removed from formulary
Prohibition to Today

• 1951 - FBN & Mr. Anslinger dismissed *La Guardia Report*
  • Cannabis consumption not a huge problem
  • Cannabis not connected to crime
  • Should not be classified as narcotic
• 1951 – *Boggs Act*
  • Mandated minimum sentencing
• *Narcotics Control Act of 1956*
  • Induced harsher sentences
Prohibition to Today

- 1960s – activists called for cannabis to be delegalized
- Vietnam veterans used for PTSD
  - Peacefulness, inhibited nightmares, created calm
- 1960s the NIH began studying cannabinoids
- 1964 – discovered the endocannabinoid system
Prohibition to Today

- 1970 – Controlled Substances Act
- Established five drug schedules
- Placed cannabis in Schedule I
- Past research deemed “folk medicine”
Prohibition to Today

- Cannabis remains a Schedule 1 narcotic
- California – Compassionate Use Act of 1996
  - Cannabis for medical use
- 2003 - NIH obtained patent for cannabinoids
  - Patent no. 6630507
  - Safe for human consumption

**United States Patent**

**Patent No.** US 6630507 B1
**Date of Patent:** Oct 7, 2003

**Inventor:** John A. Huffman, Santa Cruz, CA 95063
**Assignee:** The United States of America as represented by the Secretary of the Interior, Washington, DC 20240

**Patent No.** 6630507

**Title:** Cannabinoids as Anticipants and Methods of Use

**Patent No.**

**Date of Patent:**

**Cover Page:**

- Subject to copyright.
- This page is printed on recycled paper.
- Intellectual property rights reserved.
- Unauthorized reproduction is prohibited.

---

Pg 20
April 14, 2021: South Dakota’s overturned nonmedical (adult-use) ballot measure is currently under appeal as of March 11, 2021.

State Regulated Cannabis Programs

* = 2020 measures in Mississippi for medical use and South Dakota for nonmedical use were overturned in 2021.

01 Michigan Marijuana Laws

Michigan Regulation and Taxation of Marihuana Act of 2018

• Must be 21 years old
  • purchase, possess, and use
  • Grow 12 plants (personal)
  • 10 ounce limit
    • >2.5 ounces, locked
  • 10% tax for adult use
  • Municipalities can ban or restrict businesses

Workplace may still have zero tolerance!

MICHIGAN REGULATION AND TAXATION OF MARIHUANA ACT - Initiated Law 1 of 2018

An initiation of legislation to allow under state law the personal possession and use of marihuana by persons 21 years of age or older; to provide for the lawful cultivation and sale of marihuana and industrial hemp by persons 21 years of age or older; to permit the taxation of revenue derived from commercial marihuana facilities; to permit the promulgation of administrative rules; and to prescribe certain penalties for violations of this act. If not enacted by the Michigan State Legislature in accordance with the Michigan Constitution of 1963, the proposed legislation is to be voted on at the General Election, November 6, 2018.


local options to ban the sale of recreational marijuana
1. ECS Overview
2. Cannabinoids
3. CB1 & CB2 Receptors
Endocannabinoid System (ECS)

- Cannabinoids
  - A small molecule that modulates a receptor
  - Phytocannabinoids – found in plants (cannabis)
    - Δ9-THC, CBD, Cannabinol (CBN)
  - Endocannabinoids – made within the body
    - Anandamide (AEA), 2-arachidonoylglycerol (2-AG)
Phytocannabinoids vs. Endocannabinoids

Phytocannabinoids
The word *phyto* means coming from or related to plants.

Endocannabinoids
The word *endo* means internal or coming from within.

There are dozens of naturally occurring phytocannabinoids, while we know there are two primary endocannabinoids.

Phytocannabinoids and endocannabinoids both bind to cannabinoid receptors sites in the body.
Endocannabinoid System (ECS)

Cannabinoid Receptors
• Modulates neuron activity
  • CB1 & CB2

• Densest Concentrations
  • Cortex
  • Cerebellum
  • Hippocampus
  • Basal Ganglia

CB1
Motor activity
Thinking
Motor coordination
Appetite
Short-term memory
Pain perception
Immune Cells

CB2
Gut
Kidneys
Pancreas
Adipose tissue
Skeletal muscle
Bone
Eye
Tumors
Reproductive system
Immune system
Respiratory tract
Skin
CNS
Cardiovascular system
Liver
Endocannabinoid System (ECS)

Brain Functions Affected
• Movement
• Emotions
• Memory
• Pain
• Pleasure
• Reproduction
Cannabinoids

- Anandamide (AEA)
- THC

- Same receptors
- Intensifies sensory experience
- Stimulates appetite
- Temporarily “blots out” short-term memory
- Feelings of pleasure

- 2-arachidonoylglycerol (2-AG)
- CBD

- Same receptors
- Modulates immunity
- Regulates mood, sleep, metabolism, pain, reproduction, memory
- Works under circadian rhythm
- Neuroprotectant

Pain receptors
Perception of pain
Sleep
Anxiety
Quality of life
Medical Marijuana & CBD

1. Medical vs. Recreational Use
2. Current Evidence – Pain Management
3. Pharmacology
For example, people who use marijuana recreationally often smoke it to achieve a high, rather than to ease chronic pain or other conditions.

THC is the mind-altering chemical in marijuana primarily responsible for producing euphoria. THC-based medications are often used to increase appetite and reduce nausea. The chemical is also used to decrease pain, inflammation, and muscle control problems. That being said, not all chemicals in marijuana produce a euphoric effect. Many medical cannabis patients use the drug only for its therapeutic properties, aiming to minimize marijuana’s side effects, including the high. This is where cannabidiol, or CBD, is significant.

Cannabidiol is non-psychoactive: it does not have mind-altering effects. It also minimizes the euphoric effects of marijuana caused by THC. CBD can be useful in reducing pain and inflammation, as well as controlling epileptic seizures. It may also be effective in treating mental illness or addiction, according to the National Institute on Drug Abuse.

Recreational marijuana generally contains high levels of THC and lower levels of CBD. Medicinal marijuana is often rich in CBD, with less or no THC. Therefore, many medical marijuana users will feel the therapeutic effects without a high.
Medical Marijuana

Medical Marijuana – Most common qualifying conditions:

• ALS
• Cachexia
• Chronic pain
• Cancer pain
• Crohn disease/irritable bowel syndrome
• Epilepsy/seizures
• HIV/AIDS
• Multiple sclerosis
• Persistent muscle spasms
• PTSD
Cannabis for Pain Management

Current state of evidence – U.S.

• Conclusive or substantial evidence of effectiveness:
  • Chronic pain in adults
  • Multiple sclerosis spasticity symptoms

• Moderate evidence of effectiveness:
  • Improved sleep
  • Fibromyalgia

http://nationalacademies.org/CannabisHealthEffects

Cannabis for Pain Management

Current State of Evidence – Israel

- Chronic Pain
- Spasticity - multiple sclerosis or paraplegia
- Sleep disorders
- Psychosis
- Anxiety disorders
- Crohn’s disease

44% decrease in opioid consumption
Cannabis flowers
- Most common
  - widely available, lower cost
- Includes all cannabinoids & terpenes
  - Need chromatography lab test

Cannabis concentrates
- Vaporization or “dabbing”
- Dab = 70 – 80% concentration THC
  - Dabs, shatter, wax, budder, butane hash oil (BHO)

### Fast facts
Flower may not contain high enough concentration of cannabinoids needed for some conditions. This is why gas or liquid chromatography lab testing is so important.

A powerful strain of cannabis contains 20% THC where as a dab can reach 70-80% concentration of THC.
Cannabis Pharmacology

Smoking
- Onset: Immediate (5 – 10 min.)
- Duration: 2 – 4 hours
- Bioavailability:
  - THC = 25 – 31%
  - CBD = 13 – 19%

Patient Education
- Wait 15 min between inhalations
- Titrate for desired effect
- Do not “hold” smoke
- Water pipe & bongs – larger doses

Waiting 15 minutes between inhalation assists with the titration to desired effect – which is to relieve the targeted symptom, not the psychoactive effect. Water pipes and bongs deliver larger doses of cannabinoids per inhale than traditional smoking. Water can remove plant matter and tar. However, water that cools the smoke can trap therapeutic cannabinoids.
Vaporizers heat the oils at a lower temperature and does not burn plant matter. It is a very efficient method. Vaporizing is less likely to cause irritating respiratory side effects. Types of vaporizers include conduction (heats a metal plate), convection (hot air circulates around the plant), and oil cartridge vapor pens. The vapor pens are the least expensive option, it is discreet and easy to use. Patients can also purchase a variety of prefilled cartridges for different dosing options.
Edibles

• Onset: 1.5 – 2 hours
• Duration: 6 – 10 hours
• Bioavailability: 5 – 20%

Patient Education

• Provides stronger, longer lasting relief
  • Good for night-time dosing
• Difficult to titrate
• High risk for child accidental consumption
• Δ-9 THC conversion to Δ-11 THC is 100%

Does not provide immediate relief
Smoking results in only 20% of delta-9 THC metabolizing into delta-11 THC, ingestion results in 100%
Overconsuming edibles can lead to accidental cannabis poisoning
Candies, gummy bears, chocolates, cookies, pills, and lozenges
Oral Mucosal – tinctures, sprays, sublingual drops
  • Onset: 1 – 15 min (1.5 hours if swallowed)
  • Duration: 2 – 8 hours
  • Bioavailability: 1 – 12%

Patient Education
  • Variety of CBD:THC ratios
  • Best under the tongue or between gums & cheek
  • Avoid eating or drinking for 10 min
Cannabis Pharmacology

Topicals – creams, salves, roll-ons, pain patches
- Onset: Immediate
- Duration: 30 min – 3 hours
- Bioavailability: NA

Patient Education
- Non-psychoactive – unless VERY high THC component
- Good for localized pain
  - Arthritis, inflammation, eczema/psoriasis, chronic pain
Side Effects of Cannabis Use

Short-term side effects
- Altered senses
- Altered sense of time
- Changes in mood (suicide risk)
- Impaired body movement (fall risk)
- Impaired cognition & memory

- With high doses
  - Hallucinations
  - Delusions
  - Paranoia & psychosis

Anyone with severe diseases of the liver or kidneys should also take special precaution that the metabolic breakdown of cannabinoids does not worsen their conditions.

Individuals with a history of suicide attempt or who are at risk for suicide and those with schizophrenia, bipolar disorder, or other psychotic condition should be informed about the risks of cannabis use and be advised to not use cannabis.

The risk of suicide and cannabis use is a contentious area of study. Current findings are contradictory, and more research is needed to confirm any association between cannabis use and suicide risk while controlling for numerous confounding variables. Individuals with a greater risk of psychological disturbances and suicidal ideation should take precautions when using cannabis as a therapeutic.

Substance-induced psychosis is most frequently the result of large doses of THC. These events are typically acute and resolve quickly.

Consuming more than the recommended dose of an edible product is the leading cause of experiencing paranoia and psychosis.
Side Effects of Cannabis Use

Long-term side effects
• Clinical studies are VERY limited.

Physical effects
• Breathing problems
• Increased heart rate
• Nausea and vomiting
  • Cannabinoid hyperemesis syndrome (CHS)
• Risk of stroke

Breathing problems - Smoking marijuana may irritate the lungs. If smoked frequently, the effects are similar to tobacco smoke – daily cough & phlegm with frequent respiratory illness. Those who smoke marijuana joints tend to inhale more deeply and hold the smoke in their lungs longer. Once study documented that smoking cannabis in this way can result in 4x the exposure to carbon monoxide and 3 – 5x more tar than smoking a single cigarette. However, researchers have not identified a higher risk of lung cancer. This may be due to the interaction of cannabinoids with the endocannabinoid system.

Smoking cannabis can raise the resting heart rate for up to 3 hours, dilate blood vessels, and make the heart work harder. Smoking cannabis also decreases exercise test duration on maximal exercise tests and increases the heart rate at submaximal levels of exercise. This could be a concern for patients with a cardiac condition.

Nausea & vomiting – regular, long-term marijuana use increases the risk of developing cannabinoid hyperemesis syndrome. CHS only occurs in daily long-term users (often exceeding 3 to 5 times daily for several years). Using cannabis also affects the GI tract due to the large number of CB1 receptors in this area – potentially inhibiting gastric emptying, tightening of the pyloric sphincter, and altered motility. CHS is believed to have 3 phases – pre-emetic, hyper-emetic, and recovery. It is during the hyper-emetic phase that medical treatment is often obtained in the ED. Due to these phases, CHS is often misdiagnosed as cyclic vomiting syndrome. Of interesting note – many patients with CHS report obtaining some relief of symptoms with frequent hot showers. Discontinuing cannabis use is the only treatment of CHS.

There is limited evidence of statistical association between cannabis use and the risk of having a stroke. However, the cardiovascular effects have been proposed as a possible mechanism.
Side Effects of Cannabis Use

Consumption during pregnancy
• Delayed fetal development
  • Brain development
• Risk of low birth weight
• Risk of behavioral problems
  • Attention, memory, and problem-solving

Refrain from use if pregnant, planning pregnancy, or breastfeeding

Based on study of mothers who had used cannabis at least once per week before and throughout pregnancy versus nonusers. However, when adjusted for other drug use such as cocaine or opiates, there was no significant association between cannabis use and lowered birth rate. All studies of cannabis use and pregnancy involved women who were polysubstance drug users.
Cannabis – Drug Interactions

Hepatic/intestinal enzyme CYP3A4 metabolism

Increased level of drug
- Amiodarone
- Statins
- Pimozide
- Erythromycin
- Ketoconazole
- Verapamil
- Ritonavir
- Buprenorphine (sedation)
- Narcotics & benzos (sedation)
- Phenobarbital (sedation)

Increased effect of cannabis
- Diltiazem
- Ketoconazole
- Ritonavir
- Buprenorphine (sedation)
- Narcotics & benzos (sedation)

Cannabis Use Disorder

- DSM-V diagnosis
- Approximately 9% adults will develop CUD
- Adolescent users – increases to 17%
- Risk factors may include
  - Family or personal history of SUD
  - Low socioeconomic status
  - Traumatic childhood
  - Sexual abuse
  - Other mental health disorders

Pg 153
Long term cannabis use can potentially lead to cannabis use disorder (CUD), especially in individuals predisposed to addiction. Cannabis dependence and withdrawal is poorly understood but seems to occur with high doses taken multiple times a day. Withdrawal symptoms include irritability, nervousness, sleeping difficulties, dysphoria, decreased appetite, restlessness, strange or vivid dreams, and anxiety.
Cannabidiol - CBD

- Synergistic relationship with THC
- Types of CBD products:
  - Full-spectrum
    - Utilizes total hemp flower with all cannabinoids & terpenes
    - THC is less than 0.3%
    - Potential for positive drug test
  - Isolate
    - Pure CBD – 0% THC
    - Other cannabinoids & terpenes removed
  - Topical
    - Good for local pain targets (arthritis)

Quality varies which affects effectiveness!
Cannabidiol - CBD

- Over 100 clinical trials as of 2019 including
  - Autism spectrum disorder
  - PTSD
  - Anxiety
  - Substance use disorder
  - Chronic pain/pain
  - Epilepsy
  - Prevention of GVHD
  - Diabetes
Cannabidiol - CBD

Documented therapeutic effects:
- Anti-inflammatory
- Analgesic
- Antianxiety
- Antitumor
- Antioxidant
- Neuroprotectant
- Antidepressant
- Antiemetic
- Antipsychotic
- Inhibition of TNF-α (arthritis)
- Immunomodulatory properties
- Attenuation of fibrosis & myocardial dysfunction (diabetes)
- Inhibition of macrophage recruitment (Crohn’s disease)

TNF-α = tumor necrosis factor alpha (a cytokine, a small protein used by the immune system for cell signaling; triggers a series of various inflammatory molecules)
CBD is metabolized, among others, via the CYP3A4 enzyme. Various drugs such as ketoconazol and clarithromycin inhibit this enzyme. This leads to slower CBD degradation and can consequently lead to higher CBD doses that are longer pharmaceutically active.

The only observed side effects were reduced sucrose preference, reduced food consumption and body weight in some animals treated with CBD (50 mg/kg). CBD, which is nonhedonic, can reduce heroin-seeking behavior after, for example, cueinduced reinstatement.
CBD – Drug Interactions

May enhance sleepiness with:
- Opioids
- Benzos
- Antipsychotics
- Antidepressants
- Antihistamines
- Alcohol

Increased risk of diarrhea:
- Metformin or other diabetes medications
- Prilosec or other GERD medications
CBD is metabolized, among others, via the CYP3A4 enzyme. Various drugs such as ketoconazol and clarithromycin inhibit this enzyme. This leads to slower CBD degradation and can consequently lead to higher CBD doses that are longer pharmaceutically active.

The only observed side effects were reduced sucrose preference, reduced food consumption and body weight in some animals treated with CBD (50 mg/kg).

CBD, which is nonhedonic, can reduce heroin-seeking behavior after, for example, cueinduced reinstatement.
Epidiolex
• Only FDA-approved prescription CBD
• Treatment for seizures

Nabiximols (Sativex)
• 1:1 mix of THC and CBD
• Oromucosal spray
• Licensed in UK in 2010 (now licensed in several countries)
  • MS symptoms – bladder problems, pain, muscles spasms
  • Rheumatoid arthritis
• Investigational in the U.S.
  • Spasticity due to MS only

EPIDIOLEX is the first and only FDA-approved prescription CBD used to treat seizures associated with Lennox-Gastaut syndrome (LGS), Dravet syndrome, or tuberous sclerosis complex (TSC) in patients 1 year of age and older.

Nabilone
• Synthetic cannabinoid similar to THC

Dronabinol
• Synthetic THC
• Marinol
Summary
Summary

- Patients fear stigma with use
- Evidence of effectiveness for pain management
- “start low – go slow”
- True medical use = THC + CBD
  - No psychoactive effects
- Inpatient pain management
  - Cannabis use discontinued
  - May require increased opioid dosing
- Outpatient pain management
  - Cannabis use – decrease opioid dose
- Does have drug-drug interactions
References


References


Pennsylvania State University, College of Medicine, Department of Pharmacology. (April 2020) Cannabinoid drug - drug interactions. https://sites.psu.edu/cannabinoid


THANK YOU