Medical Cannabis for Chronic Pain

Cheryl Bernstein, MD
Associate Professor
Departments of Anesthesiology and Neurology
Division of Pain Medicine
Outline

• History medical cannabis use
• Endocannabinoid system
• Benefits and adverse effects of medicinal cannabis for pain
• Review the evidenced-based data supporting use of cannabis for chronic pain pain
• Review the Pennsylvania and UPMC Guidelines for certifying patients for medical cannabis
Early Medical Cannabis Use

• 6000 year old timeline
  • Rome, Egypt, and China

• Record of multiple medical uses
  • Epilepsy
  • Malaria
  • Tremors
  • Cough
  • Rabies
United States Pharmacopeia 1851

- Marijuana listed in 1851 US Pharmacopeia
  - Identify and standardize botanical drugs in medical use
- 1850-1937
  - Sleep
  - Appetite
  - Antispasmodic
  - Anxiolytic
  - Pain (gout, rheumatism, neuralgia)
  - Insanity
  - Symptoms of rabies
Recreational Marijuana Use

- 1900-1920 increase in recreational marijuana
  - Tied to Mexican immigration after Mexican Revolution
- Legislation against recreational use
  - States prohibit use (California--1913)
  - By 1931—29 states prohibited use
Reefer Madness 1936  
Formerly “Tell Your Children”  

- Trio of drug dealers lure teenagers to try marijuana  
  - Manslaughter  
  - Rape  
  - Hallucinations  
- Ends in “incurable insanity”
Marijuana Legislation

• 1937: Marijuana Tax Act
  • Individual possession and sale deemed illegal
  • Medicinal use remained legal but heavily taxed and regulated
  • Removed from pharmacopoeia--1942

• 1976: US Controlled Substance Act
  • Classified marijuana as a Schedule 1 drug
  • No accepted medical use and high abuse potential
  • Same category as LSD, heroin, MDMA
Cannabis and United States

- 1970 states start to decriminalize cannabis
- 1996 California 1st state approve medical cannabis
  - Compassionate Use Act
- April 2016 Medical Marijuana Act signed Pennsylvania
- 33 states and DC
  - Legalized Medical Cannabis
- 28 states and DC
  - Decriminalized marijuana and allow possession of small amounts
- 12 states legalized
  - Alaska, California, Colorado, Illinois, Maine, Massachusetts, Michigan, Nevada, Oregon, Vermont, Washington, and District of Columbia
Medical Cannabis Key Terms

- Endocannabinoid System
- Cannabinoid
- Cannabis
  - Marijuana
  - Hemp
- Cannabidiol
- Tetrahydrocannabinol
Endocannabinoid System

• Internal homeostatic system
• Critical role in the nervous system
• Regulates multiple physiologic processes
  • Pain
  • Appetite
  • Digestion
  • Mood
  • Seizure Threshold
  • Coordination
  • Immunomodulation
Endocannabinoid System

Three Components

- Endogenous cannabinoids (Anandamide and 2-arachidonoylgllycerol)
  - Endogenous agonists of receptors that also bind THC
  - Throughout the body
- Receptors
  - CBD1—central nervous system
  - CBD2—immune system
- Regulatory enzymes
  - Synthesize endocannabinoids
  - Catabolize endocannabinoids
Endocannabinoid System
Component 1: Endocannabinoids

- Anandamide and 2-arachidonoylgllycerol
- Found throughout the body
- Proposed endocannabinoid deficiency syndromes
  - Migraine
  - Fibromyalgia and Irritable Bowel Syndrome
  - Depression, Anxiety
Endocannabinoid System
Component 2: Cannabinoid Receptors

- Cannabinoid receptor type 1 (CB1)
  - Most abundant receptor
  - CNS (10x common CNS)

- Cannabinoid receptor type 2 (CB2)
  - Cells governing immune function
    - Inducible by inflammation
  - CNS (lesser extent)
Pain and Cannabinoid Receptors

• Cannabinoid receptors found in pain pathways in CNS
  • Ascending pathways (pain transmission)
  • Descending pain pathways (inhibit pain)
  • Somatosensory cortex, thalamus, amygdala
  • PAG (periaqueductal grey)
  • RVM (rostral ventral medulla)
  • Doral horn
  • Nerve terminals of sensory nerves

Pain 2003. 105:275-283
Endocannabinoid System Component 3: Regulatory Enzymes

- Enzyme to synthesize and catabolize endocannabinoids
- Catabolic enzymes
  - Metabolize anandamide and 2-AG into breakdown products
- Metabolism of cannabinoid products
  - Metabolized by CYP 450
  - Cannabinoids levels may be increased by other drugs
  - Cannabinoids can increase other drug levels
    - Coumadin
Key Terms

- Endocannabinoid System
- Cannabinoid
  - 113 cannabinoids from cannabis plant
- Cannabis
  - Hemp
  - Marijuana
- Cannabidiol
- Tetrahydrocannabinol
Cannabinoid—Any Substance That Acts on Cannabinoid Receptor

- **Phytocannabinoid**
  - Derived from cannabis plant (n=113)
  - THC (Delta-9-Tetrahydrocannabinol) and CBD (Cannabidiol)

- **Synthetic Cannabinoid**
  - Dronabinol (most common) and nabilone
  - Anorexia and nausea/vomiting

- **Endocannabinoids**
  - Anandamide and 2-AG (arachidonoylglycerol)
Key Terms

• Endocannabinoid System
• Cannabinoid
• **Cannabis**
  • Hemp
  • Marijuana
• THC
• Cannabidiol
Cannabis Plant

Cannabis (genus of flowering plants)
3 species
Indica, Sativa, Ruderalis

Hemp
Low THC < 0.3%
Fiber, Oil, Food
CBD

Marijuana
THC > 0.3%
High THC Low CBD
Key Terms

• Endocannabinoid System
• Cannabinoid
• Cannabis
  • Hemp
  • Marijuana
• Tetrahydrocannabinol (THC)
• Cannabidiol (CBD)
# CBD vs. THC

<table>
<thead>
<tr>
<th></th>
<th>Cannabidiol (CBD)</th>
<th>Tetrahydrocannabinol (THC)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Overview</strong></td>
<td>Hemp plant extract (gels, gummies, oils, etc.)</td>
<td>Psychoactive compound from cannabis plant</td>
</tr>
<tr>
<td><strong>Chemical Structure</strong></td>
<td>Similar to endocannabinoids</td>
<td>Similar to endocannabinoids</td>
</tr>
<tr>
<td><strong>Psychoactive effects</strong></td>
<td>None (minimal binding to CB1 receptors) can dampen psychoactive effects of THC</td>
<td>Binds to CB1 receptors in brain and causes euphoria</td>
</tr>
<tr>
<td><strong>Side effects</strong></td>
<td>Well tolerated</td>
<td>Increased HR, dry mouth, CNS/psych effects, slow reaction time, memory loss</td>
</tr>
<tr>
<td><strong>Drug testing</strong></td>
<td>Should not be present on routine drug testing</td>
<td>Present days to weeks after use</td>
</tr>
<tr>
<td><strong>Cannabis Plants</strong></td>
<td>Higher in hemp plant</td>
<td>Higher in marijuana</td>
</tr>
<tr>
<td><strong>Schedule</strong></td>
<td>None</td>
<td>Schedule 1</td>
</tr>
</tbody>
</table>
Why Cannabis for Pain?

• Opioid epidemic
  • Collateral effect

• Useful for variety of painful conditions
  • Refractory to other therapies

• Safe
  • Relatively few deaths reported from use

• Self titratable
Medical Cannabis: Evidence for Pain

- Experimental pain models
- Clinical studies are limited
  - Schedule I substance which is considered by DEA to have no medical use and high risk for abuse
- Evidence reviewed by National Academies of Sciences, Engineering, and Medicine
  - Reviewed of 10,700 abstracts
  - 100 conclusions on health effects of cannabis
Experimental Pain and Cannabis Dose Dependent Effect

- Inhaled cannabis on capsaicin induced pain—healthy volunteers
  - Randomized, double blind placebo controlled crossover trial (n=15)

- 4 arms
  - placebo
  - low (1 mg)
  - medium (4 mg)
  - high (7 mg)

- Low dose – no effect on pain
- Medium dose – reduced pain vs placebo
- High dose – increased pain vs placebo

Smoked Cannabis and Painful HIV Neuropathy

- Randomized controlled trial of cannabis (4% THC)
- Smoked cannabis reduced pain by 34% compared to placebo
- >30% pain reduction reported by 52%
- Reduced hyperalgesia

Medicinal Cannabis
National Academies of Science Health and Engineering

  - Review of over 10,000 abstracts
  - 100 different research conclusions (health effects and therapeutic uses)
- Therapeutic use
  - Chronic pain
  - Cancer
  - HIV—anorexia
  - IBS
  - Epilepsy
  - Neurodegenerative disorders (PD, HD, ALS)
### Medicinal Cannabis
**National Academies of Science Health and Engineering**

#### Conclusions on Therapeutic Use

<table>
<thead>
<tr>
<th>Conclusive Evidence for Effectiveness</th>
<th>Moderate Evidence for Effectiveness</th>
<th>Limited Evidence for Effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Chronic pain adults</td>
<td>• Improving short term sleep outcomes in those with OSA, fibromyalgia, chronic pain, and multiple sclerosis</td>
<td>• Appetite/ weight loss (AIDS/HIV)</td>
</tr>
<tr>
<td>• Chemotherapy induced nausea and vomiting</td>
<td>• Clinician measured spasticity in MS</td>
<td>• Clinician measured spasticity in MS</td>
</tr>
<tr>
<td>• Patient reported spasticity in multiple sclerosis</td>
<td>• Tourette syndrome</td>
<td>• Anxiety</td>
</tr>
</tbody>
</table>

The report did not conclude cannabis or cannabinoid therapies were superior to current first line therapy.
Medicinal Cannabis
National Academies of Science Health and Engineering

• Substantial evidence for the following negative effects:
  • Worsening of chronic bronchitis with cannabis smoking
  • Increased risk of motor vehicle crashes
  • Cannabis smoking and low birth weight
  • Development of schizophrenia and other psychosis
• Increased problematic use associated with the following factors:
  • male sex
  • increased frequency of cannabis use
  • cigarette smoking
  • young age
Cannabinoids for Non-Cancer Pain
Systematic Review and Meta-analysis

- 91 publications were eligible and included in the review
  - 104 distinct studies (randomized controlled and observational studies)
  - All types of cannabinoids

- 48 neuropathic pain
- 7 fibromyalgia
- 1 rheumatoid arthritis
- 48 other CNCP
  - 13 multiple sclerosis related pain
  - 6 visceral pain
  - 29 samples with mixed or undefined
Outcomes Chronic Non-Cancer Pain

• Pain intensity
  • 30% pain reduction
  • 50% pain reduction
• Physical functioning
• Emotional functioning
• Patient global impression change
• Adverse events
Moderate Evidence for Pain Reduction

RCT

<table>
<thead>
<tr>
<th>Pain Reduction</th>
<th>Cannabis</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>30% Pain Reduction</td>
<td>29.0%</td>
<td>25.9%</td>
</tr>
<tr>
<td>50% Pain Reduction (NS)</td>
<td>18.2%</td>
<td>14.4%</td>
</tr>
</tbody>
</table>

The NNTB to achieve a 30% reduction in pain for 1 person using cannabis or cannabinoids (compared with placebo groups) was estimated at 24 (95% CI 15-61)

Observational studies did not show change in pain reduction with cannabinoids vs. placebo

PAIN 159(10):1932-1954, October 2018
Patient Global Impression Change

• 4 RCTs reported PGIC as a continuous outcome on the 7-item PGIC scale

• Significant improvement among patients receiving any cannabinoid compared with placebo

Most of the evidence was for nabiximols, with some evidence for nabilone, C. sativa, and THC extract
# Results Summary

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Pooled odds ratio (95% CI)</th>
<th>Pooled event rate (%), cannabinoid vs placebo</th>
<th>Number needed to treat to benefit (NNTB) (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain outcomes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30% reduction in pain</td>
<td>1.46 (1.16-1.84)</td>
<td>29.0% vs 25.9%</td>
<td>24 (15-61)</td>
</tr>
<tr>
<td>50% reduction in pain</td>
<td>1.43 (0.97-2.11)</td>
<td>18.2% vs 14.4%</td>
<td></td>
</tr>
<tr>
<td>Patient global impression of change</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perceived “much” to “very much” improved</td>
<td>1.62 (1.34-1.96)</td>
<td>18.9% vs 11.8%</td>
<td>38 (27-62)</td>
</tr>
<tr>
<td>Adverse events</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All-cause adverse events</td>
<td>2.33 (1.88-2.89)</td>
<td>81.2% vs 66.2%</td>
<td>6 (5-8)</td>
</tr>
<tr>
<td>Study withdrawals—adverse events</td>
<td>3.47 (2.64-4.56)</td>
<td>15.8% vs 4.5%</td>
<td>40 (35-49)</td>
</tr>
</tbody>
</table>

Bold font indicates a statistically significant result. Only categorical outcomes with a moderate or higher GRADE rating are reported here.

* Number needed to treat to benefit unable to be calculated as the pooled odds ratio crossed the line of no effect.

CI, confidence interval.
Cannabis and Patient Satisfaction

• Evaluated response to medical cannabis and patient satisfaction for chronic pain
• 83 patients included
  • Patient impression of change
  • Satisfaction
  • Changes in pain, sleep, anxiety and depression
  • Medication tapering

Cannabis and Chronic Pain

- Percent of patients reaching response thresholds
- Majority of patients reaching meaningful response for impression of change, anxiety and sleep
- Higher than general UPMC Pain population

Cannabis Satisfaction Rates in Chronic Pain Patients.
American Academy Pain Medicine 2020
Contraindications

- Schizophrenia or psychotic illness unless collaboration with treating psychiatrist
  - 1st degree relative with psychotic illness
- Cardiovascular risk
  - May cause vasodilation and should be avoided in those with active, unstable ischemic heart disease
- Pregnancy or breastfeeding
Cannabis and Medical Co-Morbidities

• Caution in those with renal or hepatic disease
• Avoid smoking or vaporization especially in those with pulmonary disease
• Caution use in those with current or history of substance use disorder
• Cautious use with other sedative or psychoactive medications
  • Tapering opioids in those with cannabis use
Cannabinoids and Older Adults

- Elderly metabolize drugs more slowly
- Low and slow
- Caregiver monitoring
- Increase susceptibility to falling
  - Orthostatic hypotension
  - Sedation
  - Weakness
  - Spatial and visual distortion
Driving Recommendations

- Most frequently reported drug (after alcohol) found in connection with MVAs, including fatalities
- Discuss with patients that use of medical marijuana is associated with a higher rate of motor vehicle accidents.
- Do not drive for at least 6-8 hours after the first dose
- Risk of MVA:
  - Doubles when a person drives within an hour of using marijuana
  - Increases 5x for drivers with a BAL above 0.08%
Problematic Use of Opioids vs. Medicinal Cannabis

• Assess problematic use of prescription opioids vs. medical cannabis

• 888 individuals treated with opioids or MC

• Problematic use of prescription opioids and MC
  • DSM-IV criteria, Portenoy’s Criteria (PC), Current Opioid Misuse Measure (COMM) questionnaire

• Problematic is common among chronic pain patients treated with prescription opioids
  • Higher than with MC

Problematic Use of Opioids vs. Medicinal Cannabis Chronic Pain

• Problematic use of opioids is common among chronic pain patients treated with prescription

• Opioid misuse is more prevalent than problematic use of cannabis among those receiving MC

Cannabis Hyperemesis Syndrome

• Described by Allen et al. 2004
• Cyclic hyperemesis with chronic long-term cannabis
• Relieved by bathing or showering in hot water
• Resolution of symptoms with cessation of cannabis use
Guidelines for Medical Cannabis

Salient Points

• Provider-patient relationship
• Clinical history—qualifying medical condition
  • Previous therapies
  • Substance abuse
  • Psychotic illness
  • Risk assessment

• Consent/agreement
  • Risk/benefit
  • Not FDA approved
  • Lack of rigorous study
  • Discussion of other options
  • Effect of ability to operate heavy machinery
  • Legal guardian in case of minor

• Urine toxicology

Guidelines for Certification

• Check PDMP
  • Controlled substance use
  • Avoid or decrease concurrent opioid use
• Referral to consultants for those at high risk
• Substance or mental health disorder
  • Psychiatrist
  • Addiction specialist
True or False?

• Physicians in Pittsburgh prescribe marijuana.
• Prescribing a Schedule I substance is a violation of federal law
• Recommending/Certifying marijuana is allowed
• Physicians may not be prosecuted for recommending marijuana to Qualified Patients
  • Practitioners who recommend marijuana without a “good faith” medical basis will face criminal liability
  • Follow guidelines

False
Each state has the same qualifying conditions for medical cannabis use.

Some states require providers to register with state or oversight agency
  - Provide information when a patient is recommended
  - Notification of adverse effects

Pennsylvania Medical Marijuana Program 4-hr Required Course
  - Approved by the Pennsylvania Department of Health (PADOH)
## Qualifying Conditions in Pennsylvania

<table>
<thead>
<tr>
<th>ALS</th>
<th>Epilepsy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiety</td>
<td>Glaucoma</td>
</tr>
<tr>
<td>Autism</td>
<td>HIV/AIDS</td>
</tr>
<tr>
<td>Cancer</td>
<td>HD</td>
</tr>
<tr>
<td>Crohn’s</td>
<td>Inflammatory bowel disease (Crohn’s or ulcerative colitis)</td>
</tr>
<tr>
<td>Diskinetic disorders</td>
<td>Intractable seizures</td>
</tr>
<tr>
<td>Damage to the nervous tissue of the spinal cord with objective neurological indication of intractable spasticity</td>
<td>Multiple Sclerosis</td>
</tr>
<tr>
<td>Neurodegenerative disorders</td>
<td>Neuropathies</td>
</tr>
<tr>
<td></td>
<td>Opioid Use Disorders</td>
</tr>
<tr>
<td></td>
<td>PD</td>
</tr>
<tr>
<td></td>
<td>PTSD</td>
</tr>
<tr>
<td></td>
<td>Severe chronic or intractable pain of neuropathic origin or severe chronic or intractable pain in which conventional therapeutic intervention and opiate therapy is contraindicated or ineffective.</td>
</tr>
<tr>
<td></td>
<td>Sickle Cell Anemia</td>
</tr>
<tr>
<td></td>
<td>“Terminally ill.” A medical prognosis of life expectancy of approximately one year or less if the illness runs its normal course.</td>
</tr>
<tr>
<td></td>
<td>Tourette’s Syndrome</td>
</tr>
</tbody>
</table>

Epilepsy

Glaucoma

HIV/AIDS

HD

Inflammatory bowel disease (Crohn’s or ulcerative colitis)

Intractable seizures

Multiple Sclerosis

Neurodegenerative disorders

Neuropathies

Opioid Use Disorders

PD

PTSD

Severe chronic or intractable pain of neuropathic origin or severe chronic or intractable pain in which conventional therapeutic intervention and opiate therapy is contraindicated or ineffective.

Sickle Cell Anemia

“Terminally ill.” A medical prognosis of life expectancy of approximately one year or less if the illness runs its normal course.

Tourette’s Syndrome
True or False

- Cannabis is FDA approved. **False**
- Epidiolex
  - FDA approved pure CBD product for Dravet syndrome and Lennox-Gastaut syndrome
- FDA approved synthetic cannabinoids
  - Dronabinol (Marinol and Syndros)—chemotherapy induced N/V and AIDS related anorexia
  - Nabilone (Cesamet)—chemotherapy induced N/V
True or False

- Cannabis is a first line treatment for some conditions.
- Evidence from RCT to support effective treatment for some conditions
- Effect no superior to current 1st line therapies
- Should be considered if other treatments fail

False
Certification Attestation

1. I have conducted a patient consultation in a manner appropriate to make a medical determination as to the patient’s serious medical condition(s) indicated above.

2. I have made a diagnosis of a serious medical condition for the above patient for which the patient will receive a therapeutic or palliative medical benefit from the use of medical marijuana.

3. I have established a medical record for the patient and shall maintain that medical record while the patient is under my continuing care treatment.

4. I have consulted the Prescription Drug Monitoring Program database to review whether the patient has been recently dispensed any controlled substances that would prohibit or pose a risk for the patient to obtain medical marijuana.

5. I have received an informed consent statement from the patient, or if applicable, an informed consent statement from the patient’s caregiver, custodial parent, legal guardian or spouse that includes an explanation of the potential risks and benefits of the medical use of marijuana.
Moving Forward: Information, Policy & Guidelines

- Patients must pay $50 and register on the state website
- [https://www.pa.gov/guides/pennsylvania-medical-marijuana-program](https://www.pa.gov/guides/pennsylvania-medical-marijuana-program)
- Insurance does not cover cost of medical marijuana (possibly hundreds of dollars per month)
- Patients are not certified indefinitely – this can be specified by the provider on a case-by-case basis
Variable Effects of Cannabis

- Dose
- Ratio of cannabinoids
- Route
- Timing
- Health status and age
- Co-administration
- Prior cannabis use
- Environmental factors (setting of use)

Recommend consultation with dispensary pharmacist
# Common Modes of Administration

<table>
<thead>
<tr>
<th>Vaporization</th>
<th>Oral</th>
<th>Oromucosal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychoactive effects 90 seconds</td>
<td>Psychoactive effects in 90 minutes</td>
<td>Psychoactive effects 30 minutes-2.5 hours</td>
</tr>
<tr>
<td>Max 15-30 minutes</td>
<td>Peak 2-3 hours</td>
<td>Peak effect as early 1.5 hours</td>
</tr>
<tr>
<td>Subside 2-3 hours</td>
<td>Last 4-12 hours</td>
<td></td>
</tr>
<tr>
<td>Similar to smoking</td>
<td>Delayed onset</td>
<td>Lower levels of THC compared to smoking</td>
</tr>
<tr>
<td>Amount dependent on temperature, duration</td>
<td>May be difficult to regulate dosage (first pass)</td>
<td>Because some is swallowed the effects may be delayed</td>
</tr>
<tr>
<td>and volume of vaporization</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Easier titration for acute symptoms</td>
<td>Longer duration for chronic pain</td>
<td>Desirable for treating nausea</td>
</tr>
</tbody>
</table>

Often recommend 5mg oral cannabis twice daily or cannabis tincture (1:1 THC/CBD ratio). Topical cannabis for those susceptible to side effects.
Dispensaries

• Only can purchase from state-approved dispensaries which...

• Can only supply products from within-state approved farms

• Pills, digestibles (but not edibles), sublingual oils, topical oils, and vaping products can be dispensed

• Not currently entered into PDMP, but an alternate state database
<table>
<thead>
<tr>
<th>Product</th>
<th>Quantity</th>
<th>Price</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alien Bubba Sugar</td>
<td>1g</td>
<td>80.00</td>
</tr>
<tr>
<td>Pineapple Express</td>
<td>1g</td>
<td>80.00</td>
</tr>
<tr>
<td>E-Liquid Cappuccino Pen</td>
<td>1g</td>
<td>30.00</td>
</tr>
<tr>
<td>Cinderella 99</td>
<td>1g</td>
<td>70.00</td>
</tr>
<tr>
<td>Island Sweet Skunk Liquid</td>
<td>1g</td>
<td>60.00</td>
</tr>
</tbody>
</table>
Uncertainties

• Treatment decisions will be left to the medical staff at the dispensary
  • Physicians may specify recommendations but control over product is limited

• Best dosing practices are unknown
  • University of Pittsburgh Pharmacy School is working on a process to “approve” dispensaries
  • 1:1 THC/CBD balance side effects and analgesia
  • 4% vaporization good analgesia

• Dispensaries may not carry the desired cannabis preparation
Summary

• Cannabis may be an effective treatment for chronic pain (neuropathic pain, cancer pain, MS pain)
  • As part of multimodal treatment plan
  • To aid with medication taper
  • With careful patient selection
  • Requires close monitoring and consent

• Improvements in pain, sleep and mood
  • High patient satisfaction

• Further research and standardization is needed