Cannabinoids in Palliative Medicine

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PALLIATIVE CARE
Definition: Palliative Care

Palliative Care is an approach that improves the quality of life of patients and their families facing the problem associated with lifethreatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psycho - social and spiritual.

WHO 2002
Palliative Care

What do palliative patients expect?

S  Good symptom control
E  Decisions: mostly shared decision making
N  Networking: cooperation of the professionals, proxies and the volunteers
S  Support for the teams and the proxies

=> But it begins mostly with good symptom control
PAIN
Cannabinoids for the Treatment of Chronic Non-Cancer Pain: An Updated Systematic Review of Randomized Controlled Trials

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Abstract An updated systematic review of randomized controlled trials examining cannabinoids in the treatment of chronic non-cancer pain was conducted according to PRISMA guidelines for systematic reviews reporting on health care outcomes. Eleven trials published since our last review met inclusion criteria. The quality of the trials was excellent. Seven of the trials demonstrated a significant analgesic effect. Several trials also demonstrated improvement in secondary outcomes (e.g., sleep, muscle stiffness and spasticity). Ad-

Introduction

Chronic pain is a growing public health problem affecting approximately one in five people and predicted to increase to one in three over the next two decades (Blyth et al. 2001; Moulin et al. 2002; Breivik et al. 2006). The prevalence of chronic pain is likely to increase as the population ages and as medical advances continue to improve survival related to cancer, serious injury and dis-
Pain: knowledge

Clinical Crossroads

Medical Marijuana for Treatment of Chronic Pain and Other Medical and Psychiatric Problems
A Clinical Review

Kevin P. Hill, MD, MHS

IMPORTANCE As of March 2015, 23 states and the District of Columbia had medical marijuana laws in place. Physicians should know both the scientific rationale and the practical implications for medical marijuana laws.

OBJECTIVE To review the pharmacology, indications, and laws related to medical marijuana use.

EVIDENCE REVIEW The medical literature on medical marijuana was reviewed from 1948 to March 2015 via MEDLINE with an emphasis on 28 randomized clinical trials of cannabinoids as pharmacotherapy for indications other than those for which there are 2 US Food and Drug Administration–approved cannabinoids (dronabinol and nabixim), which include nausea and vomiting associated with chemotherapy and appetite stimulation in wasting illnesses.

FINDINGS Use of marijuana for chronic pain, neuropathic pain, and spasticity due to multiple sclerosis is supported by high-quality evidence. Six trials that included 325 patients examined chronic pain, 6 trials that included 396 patients investigated neuropathic pain, and 12 trials that included 1600 patients focused on multiple sclerosis. Several of these trials had positive results, suggesting that marijuana or cannabinoids may be efficacious for these indications.

CONCLUSIONS AND RELEVANCE Medical marijuana is used to treat a host of indications, a few of which have evidence to support treatment with marijuana and many that do not. Physicians should educate patients about medical marijuana to ensure that it is used appropriately and that patients will benefit from its use.

Pain: pathophysiology

Folie übernommen von Ruscheweyh ismed 2011 Handout.pdf
Schmerzreiz

nozizeptive Rezeptoren

5-HT

NA

Opiode

präfrontaler Cortex
ACC
Insula
Amygdala
Hypothalamus

PAG
RVM
Locus coeruleus

Valet et al. 2004 Pain 109:399

Tracey et al. 2002 J Neurosci 22:2748
Pain therapy in palliative medicine: expert’s opinion

Cannabionoids play a little but interesting role for pain therapy in palliative medicine

– In specific (e.g. MS, ALS) diseases cannabinoids might be helpful

– Pathophysiology of pain is very diverse

– We know too little about which cannabinoid for which pain

– Goal is: clear in mind and low in pain
NAUSEA & VOMITING
Nausea & vomiting: knowledge

Limited evidence is available to support the use of cannabis-based medicines (dronabinol, nabilone, THC) in multifactorial nausea in advanced cancer patients.

Cannabinoids (nabilone, dronabinol, THC) are comparable to standard antiemetics for chemotherapy-induced nausea and vomiting that were used before the development of 5-HT3 antagonists (mostly prochlorperazine, chlorpromazine, domperidol).

Limited evidence is available to support the use of cannabis-based medicines in the therapy of radiotherapy-related
Nausea & Vomiting: Literature


Nausea & vomiting: pathophysiology

**GABA, ua.**

**μ (MOR)**
Enkephaline

**M1, H1, 5HT2, CB1**

**D2, 5HT3**

**H1, M1**

**M1, H1, 5HT3, NK1, D2?, NMDA?**

**5HT3, 5HT4, NK1, NK3, M1, D2, Motilin**
Mechanorezept

**5HT3**
Mechanorezept
Nausea & vomiting: expert’s opinion

Cannabinoids have a place in the era of modern antiemetic medication for palliative patients with refractory nausea and vomiting (Case reports for otherwise therapy refractory nausea)

Further research is warranted which cannabinoid for which situation
ANOREXIA & CACHEXIA
Anorexia & cachexia: knowledge

The use of cannabis-based medicines for anorexia and cancer cachexia is at present still unclear, since results of trials were heterogeneous and trials were criticised for methodology (including heterogeneity in stages of cachexia and use of cannabinoids).

THC showed some evidence in weight gain in patients with HIV/AIDS (but megestrol was better), limited evidence suggested increased appetite.
Anorexia & cachexia: literature


Anorexia & cachexia: pathophysiology

Involvierte pathogenetische Mechanismen:

– Entzündung
– Neuro-hormonelle Veränderungen
– Hypermetabolismus
  (diese sind nicht gänzlich von einander zu trennen)

Führen zu:

– Inappetenz, vermindelter Nahrungszufuhr
– Kataboler Stoffwechsellage
– Muskelabbau: vermindelter Muskelmasse und -kraft
## Tumorkachexie: Stadieneinteilung
adaptiert nach Fearon K (2011) Lancet Oncology

<table>
<thead>
<tr>
<th>normal</th>
<th>Präkachexie</th>
<th>Kachexie</th>
<th>Refraktäre Kachexie</th>
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<td>Monitoring Präventive Interventionen</td>
<td>Tumorthherapie, Multimodales Management, Ernährungstherapie</td>
<td>Symptomkontrolle</td>
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</table>

- Gewichtsverlust <5%
- Gewichtsverlust > 5% in 6 Monaten oder BMI < 20 und Gewichtverlust > 2%
- Anorexie
- Häufig reduzierte Nahrungszufuhr
- metabolische Veränderungen: Insulinresistenz, pathologische Glucosetoleranz
- Systemische Entzündung
- SW katabol und Tumor non-reponsiv auf Therapie tiefer Funktionsst. WHO 3 o. 4 Erwartete Lebensdauer < 3 Mt
Anorexia & cachexia: expert’s opinion

• In early stage of cachexia: cannabinoids might be helpful
• In late stage of tumor cachexia: cannabinoids might have little to no effect
• In respect to pathophysiology:
  – CBD is more promising than THC in late stage of tumor cachexia
  – Cannabinoids might have more effect on anorexia than on cachexia
• In patients with HIV/AIDS with cachexia and cardiovascular risk factors we have to think about cannabinoids
CANNABIONOIDS: LAST HOPE
Cannabinoids: last hope

Many patients contact us with the question of cannabinoids as tumorspecific therapy

– We aren’t as far yet
– We shouldn’t create illusion that cannabinoids stop or even cure cancer
– If we «try» a tumor-specific therapy with cannabinoids we should do it in research trials
BARRIERS TO CANNABINOIDS IN PALLIATIVE MEDICINE
Why are cannabinoides so rarely used in Swiss Palliative Care

Administrative barriers
   – Palliative medicine => reacts quickly on situations

Knowledge barriers
   – We aren’t used to use cannabinoids

Patient’s barriers are less often than barrierers of professionals
   – We are more often asked by patients if we could use cannabinoids than we offer cannabinoids to them
OUTLOOK
Visions

• Good research with good concepts
• Cannabionoids as accepted drugs
• Good networking