UPMC PALLIATIVE AND SUPPORTIVE INSTITUTE

THE TABLET: PALLIATIVE CARE PHARMACY TIPS

October 8, 2021 Vol. 1, No. 25

Palliative Care Pharmacy Team:

Clinical Pharmacy Specialist:

Maria Felton Lowry, PharmD, BCPS, BCGP
Assistant Professor
University of Pittsburgh School of Pharmacy, Department of Pharmacy and Therapeutics
Palliative Care Clinical Pharmacy Specialist
UPMC Palliative and Supportive Institute

Cell: 412-627-8473
Office: 412-864-2899
Email: lowrymf@upmc.edu

If you have a topic you would like the pharmacy team to answer, please send your suggestions to: lowrymf@upmc.edu

TODAY'S TOPIC:

Medical Cannabis for Pain, Review of the Evidence

Background:

Cannabis plant contains phytocannabinoids, which have been found to have a wide array of potential therapeutic uses. The two most studied are 9-tetrahydrocannabinol (THC), the psychoactive component, and cannabidiol (CBD). These phytocannabinoids bind to a variety of receptors and locations for analgesic effect. 36 states have legalized cannabis for medical use, including Pennsylvania. In PA, severe or intractable pain, is one of the numerous serious medical conditions listed that could qualify patients for medical cannabis. It is available in PA in a variety of formulations in dispensaries across the state such as: oil, pill, tincture, nebulizer, vaporization, topical, and liquid. Federally, cannabis is still considered a Schedule 1 substance as defined by the Controlled Substance Act of 1970 so limitations with researching medical cannabis use and efficacy exists.

Importance:

Medical cannabis use is growing in our palliative care population for chronic pain. It is important for palliative care clinicians to be aware of the available (but likely limited) evidence for medical cannabis use in our patient population for pain.

The Literature:

Pain. 2021 Jul 1;162(Suppl 1):S67-S79.

Cannabinoids, cannabis, and cannabis-based medicine for pain management: an overview of systematic reviews (Moore)

Objective: To assess the methodological quality, scope, and reported results of systematic reviews and meta-analyses of RTCs of cannabinoids for pain relief

Methods:

- Literature review through January 2020
- Systematic reviews of RCTs including people of any age with any form of acute and chronic pain receiving any type of cannabinoid product (natural or synthetic), cannabis, or CBM, any route of administration, any dose, with any comparison
- Assessment of review quality by 16-criterion AMSTAR-2 method, low ratings generally resulted in low assessments in overall confidence in the results of the review

Outcomes:

- Analgesic efficacy, definitions varied across studies

Results:

- 57 systematic reviews included (published between years of 2001-2019)
- Types of pain included: chronic noncancer (n=8), neuropathic (n=10), cancer only (n=7), all pain (n=10)
- Cannabinoid preparations varied among studies: cannabinoid, any cannabis preparation, plant-based cannabis preparation, nabilone, dronabinol, nabiximols, THC, cannabis sativa, cannabidiol
- Route of administration was not generally defined, in those that were: "any route" was most common, followed by oral or topical, and smoked or inhaled
- Only 4 of the Quality Criteria were met by more than half of the reviews
- OF the 17 reviews attempting a numerical calculation of the magnitude of analgesic effect, 9 had a positive and 5 a negative recommendation
- Low quality systematic reviews exist for cannabinoids for chronic pain

Discussion:

- No review examined the effects of a particular cannabinoid, at a particular dose, using a particular route of administration, for a particular pain condition, reporting a particular analgesic outcome

Conclusion:

- Current reviews are mostly lacking in quality and cannot provide a basis for decision-making. A new high-quality systematic review of randomised controlled trials is needed to critically assess the clinical evidence for cannabinoids, cannabis, or CBM in pain

This conclusion leads us to the next article… a new systematic review on cannabinoids for pain management

Pain. 2021 Jul 1;162(Suppl 1):S45-S66.

Cannabinoids, cannabis, and cannabis-based medicine for pain management: a systematic review of randomized controlled trials (Fisher)

Objective: Provide comprehensive summary of the evidence from primary RCTs of cannabinoids, cannabis, and CBM for pain management

Methods:

- Literature review through January 2020
- People with acute or chronic pain, not limited to adults (children included), included only trials that retained 30 participants/arm or more at posttreatment
- Any type of cannabinoid product (natural or synthetic), any route of administration compared to any control (placebo versus active pain treatment)

Outcomes:

- Primary: Proportion of people with at least 30% pain intensity reduction/moderate improvement, proportion of people with at least 50% pain intensity reduction/substantial improvement
- Secondary: continuous pain intensity measurements, physical functioning, emotional functioning, quality of life, adverse events, onset/duration analgesia, sleep duration/quality, requirement for rescue analgesia

Results:

- N= 36 RCTs, average age of participants = 51
- Neuropathic pain (n=13), acute pain after surgery (n=4), multiple sclerosis (n=10), chronic prostatitis/chronic pelvic pain, carpal tunnel syndrome, and back pain (n=1)
- Efficacy
    - Separated analysis based on cannabis product used and pain type
    - Naxibimols delivered for longer than 1 week showed small beneficial effects for 30% reduction in pain intensity and change in pain intensity scores. They are beneficial for improving physical function and sleep quality.
    - No beneficial effect in favor of cannabinoids found when differentiated by type of pain, with the exception of possible benefit in setting of neuropathic pain
    - Two primary outcomes of reduction in pain intensity 30% and 50% depicted below

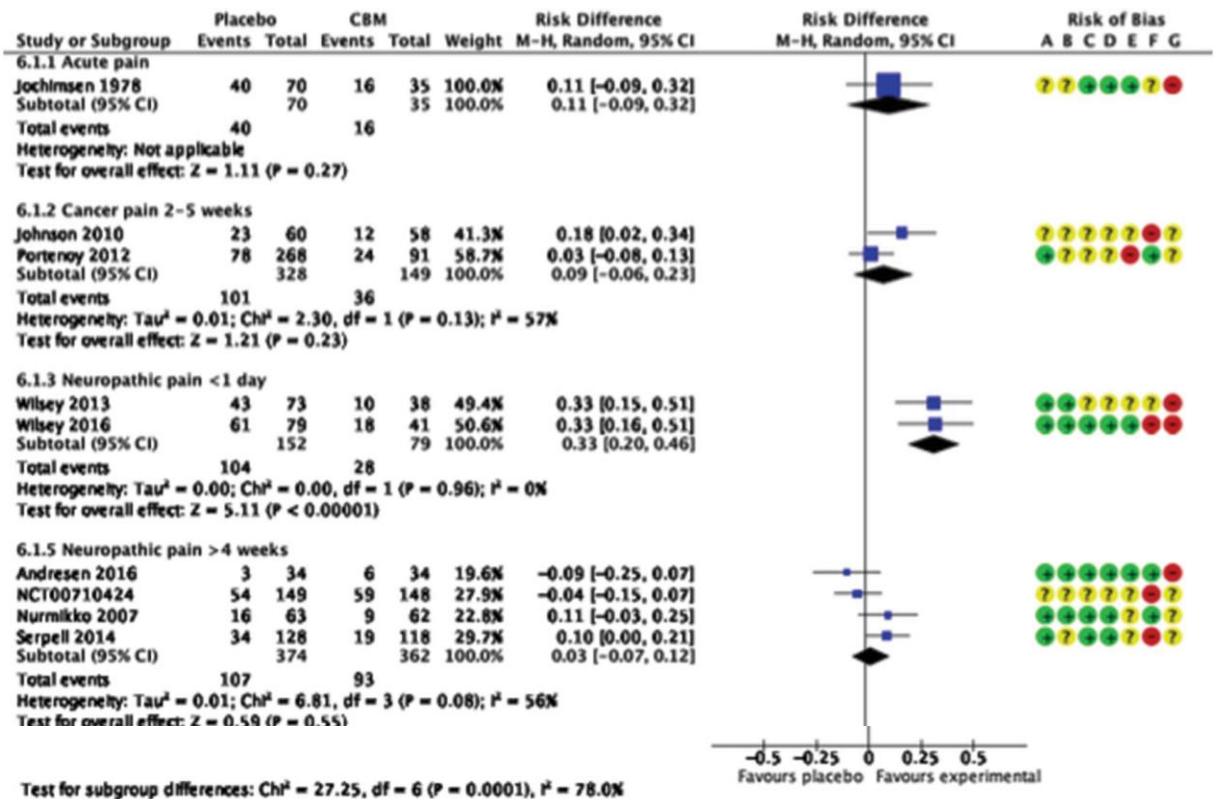
CLINICAL PEARL: Limited, low quality, evidence exists for the efficacy of medical cannabis for the treatment of pain.

UPMC PALLIATIVE AND SUPPORTIVE INSTITUTE

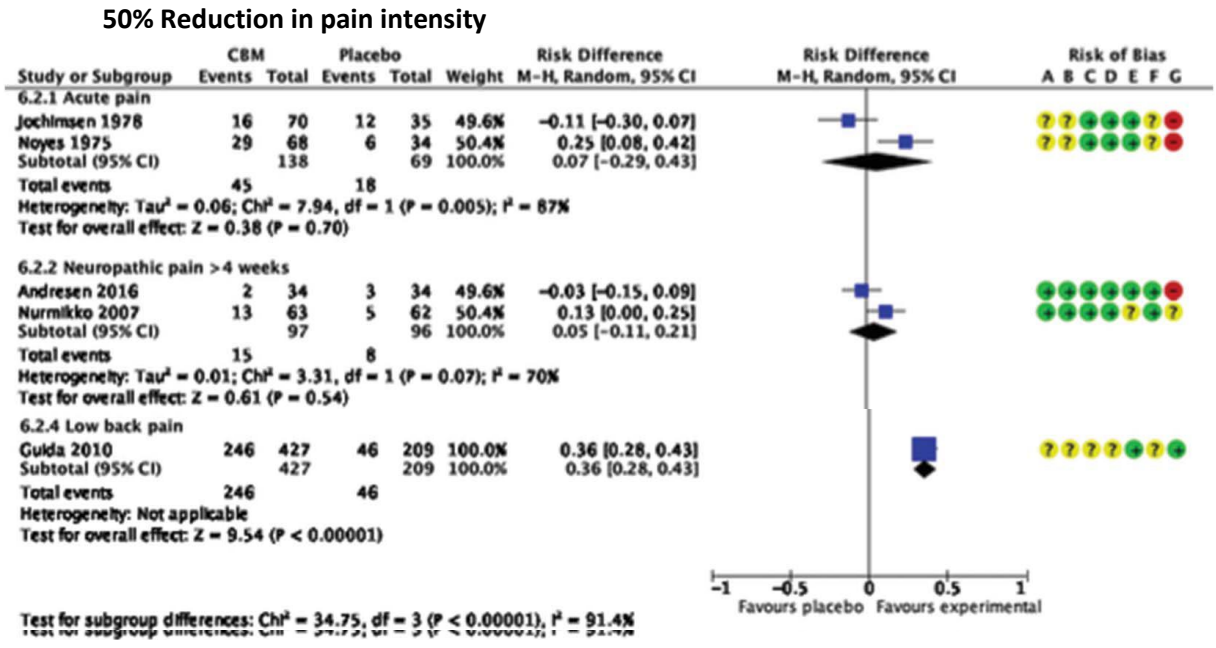
THE TABLET: PALLIATIVE CARE PHARMACY TIPS

October 8, 2021 Vol. 1, No. 25

30% Reduction in pain intensity (sorry for the poor quality of the figure… it's this way in the original article)



50% Reduction in pain intensity



- Safety
  - Adverse effects were not listed
  - Generally speaking, those patients who received cannabis, CBM, or cannabinoid reported either no difference or experienced more adverse effects that compared to a control group

Discussion:

- No studies included had low risk of bias

Conclusion:

- RCT evidence base for using cannabinoids, cannabis, and CBM is of low or very low quality

Bottom Line:

- Phew.. this was a lot to digest. All in all, the body of evidence for medical cannabis used for pain is generally low-quality evidence
- It is really hard (or almost impossible) to compare studies as there is no standard formulation, route, dose; therefore it is really difficult to include such studies in a systematic review
- It is important to consider the quality of systematic reviews when considering their implications for clinical practice, this applies to any/all systematic reviews, not limited to medical cannabis literature. The first review highlighted the importance of this issue.
- Long-term safety and efficacy data is lacking
- Systematic reviews with heterogenous studies included don't really tell us much. It's hard to compare trials that include unique formulations, doses, concentrations, and outcomes, such as those that exist for medical cannabis, like mentioned above.
- When evaluating literature for medical cannabis efficacy for pain (and other outcomes) it is probably better to stick with individual RCTs at this point in time until there is way to systematically compare similar pharmacologic compounds and outcomes… systematic reviews aren't *always* better…
- Medical cannabis may work for certain patients with certain pain syndromes depending on their goals of care and functional outcome goals
- It is important to tell patients that one size does not fit all in terms of the use of medical cannabis for pain management and it may come down to some trial and error with formulation, concentration/dose, etc…

CLINICAL PEARL: Limited, low quality, evidence exists for the efficacy of medical cannabis for the treatment of pain.