UPMC PALLIATIVE AND SUPPORTIVE INSTITUTE

THE TABLET: PALLIATIVE CARE PHARMACY TIPS

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

TODAY'S TOPIC:

Literature Spotlight: Cannabidiol (CBD) Oil in Palliative Care

Background:

Medical cannabis is becoming increasingly popular, given changes in state-level policies surrounding its use for medical purposes for serious medical conditions. The major cannabinoids are: cannabidiol (CBD) – non-psychoactive, and tetrahydrocannabinol (THC) – psychoactive. Different combinations of these cannabinoids are utilized for symptom management; THC is thought to be responsible for symptom mitigation more so than CBD. Mixed evidence exists for medical cannabis's use as an analgesic, anxiolytic, antiemetic, appetite stimulant, and sleep aid given the difference in formulations and concentrations of THC/CBD within the individual products studied. Additionally, cannabis is still considered a Scheduled I drug on the federal level, which complicates clinical research process.

The State of Pennsylvania allows medical cannabis in 7 formulations: pill, oil, tincture, liquid, topical forms, vaporization and nebulization. Within UPMC at Presbyterian-Shadyside, a policy exists surrounding inpatient medical cannabis use which can be found here: UPMC Policy CP-75

Importance:

Many of our patients consider utilizing medical cannabis to mitigate symptoms associated with their life-limiting illnesses. It is important for palliative care clinicians to be aware of the ever-evolving data in this area. We will review a recent RCT done within palliative care population and compare to existing evidence.

The Literature:

J Clin Oncol. 2023 Mar 1;41(7):1444-1452.

Phase IIb randomized, placebo-controlled, dose-escalating, double-blind study of cannabidiol oil for the relief of symptoms in advanced cancer (MedCan1-CBD)

Objective: to assess whether CBD oil, when used in conjunction with standard palliative care, reduced symptom burden in patients with advanced cancer

Methods: phase IIb, randomized, dose-escalated placebo-controlled study across 5 tertiary medical centers in Australia

- Adults (> 18 years old) with advanced cancer and a total symptom distress score (TSDS) as measured by ESAS of ≥ 10/90 (with at least one symptom score ≥ 3) with a performance status ≥ 30 (Australian-modified Karnofsky Performance Scale)
- CBD oil 100mg/mL versus placebo plus standard palliative care in both groups
- Dose titration occurred every 3rd day over 14 days from 0.5mL (50mg) once daily to 2mL (200mg) TID and could continue for an additional 14 days (optional)

Outcomes:

- Primary: ESAS Total Symptom Distress Score (TSDS) at day 14 compared to baseline
- Secondary: Patient-determined effective dose, ESAS TSDS at days 7, 21, and 28, physical and emotional ESAS subscores, individual symptom scores, OME (oral morphine equivalent) at baseline and weekly, Global Impression of Change; depression and anxiety score, quality of life (QoL), and adverse events

Results: n=142, mean age: 64.6 years (SD 12.8), 52.8% male

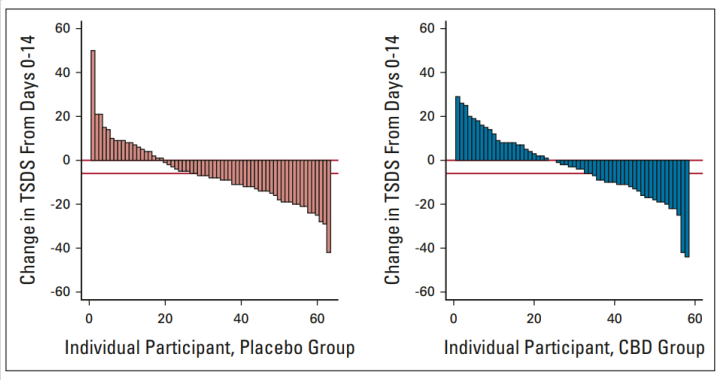

FIG 2. Proportion of responders (fall in TSDS ≥ 6 between baseline and day 14) in each arm (placebo: 37 of 63 [58.7%]; CBD: 26 of 58 [44.8%], $P = .13$). CBD, cannabidiol; TSDS, total symptom distress score.

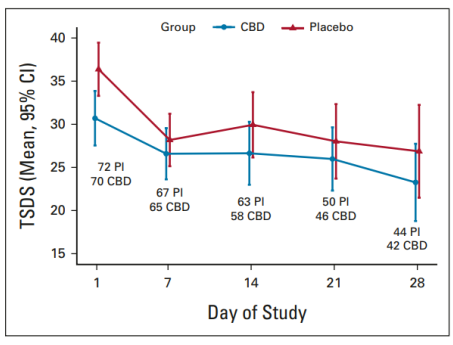

FIG 3. TSDS over time. PI and CBD indicate the number of participants at each time point. Change per day 0.1 (95% CI, −0.06 to 0.26), $P = .21$. Note missing data at days 7 (2), 21 (2), and 28 (1). CBD, cannabidiol; PI, Placebo; TSDS, total symptom distress score.

- Median final volume of medication taken per day at day 14 was 6mL for placebo and 4mL (400mg) for CBD
- Most participants in both arms (53% CBD and 65% placebo) reported feeling better or much better at days 14 and 28 (70% and 64%)
- No detected difference between arms in change of OME from baseline (mean baseline OME: 50mg (0-590mg))
- No difference between groups for depression, anxiety and stress scores or quality of life
- Most common ADE: somnolence and abdominal pain in CBD group

Conclusion: "CBD oil did not add value to the reduction in symptom distress provided by specialist palliative care alone."

J Pain Symptom Manage. 2022 Nov;64(5):e260-e284.

Cannabis in palliative care: A systematic review of the evidence

Methods: Literature review 1960-Sept 2021

Results: n=52 studies (20 randomized, 32 non-randomized)

- Cancer (n = 4491), dementia (n = 43), AIDS (n = 235), spasticity (n = 16), NORSE syndrome (n = 1) were included.
- Heterogeneity in cannabis products studied (CBD, CBD/THC, THC)
- The quality of evidence: 'very low' or 'low' for all studies
- Positive treatment effects (statistical significance with $P < 0.05$) were seen for *some* MC products
  - ***Cancer***: pain, nausea/vomiting, appetite, sleep, fatigue, chemosensory perception and paraneoplastic night sweats; ***Dementia***: appetite and agitation; ***AIDS***: appetite, nausea/vomiting
- Meta-analysis was unable to be performed due to inability to compare cannabis products and study outcomes

Bottom Line:

- Of note in the RCT, CBD was utilized without THC; THC is thought to provide most of the symptom management relief effects which may account for the lack of difference between groups
- Total symptom burden was not different between groups; however, we do not know if certain symptoms outside of anxiety/depression/stress were individually affected (ie. nausea, pain, insomnia) given the primary outcome of total symptom burden reduction on the ESAS
- Prior studies showed a 6-point improvement in total ESAS scores to be clinically significant. This was found in both groups receiving **palliative care**! Although no difference between CBD vs placebo
- It is difficult to make blanket statements about efficacy of medical cannabis when a patient can go to a dispensary and get different strains and combinations of THC/CBD. Some products are likely be more effective than others for certain symptoms associated with serious illness.
- It is not unreasonable to have patients try medical cannabis products to see if one ends up being effective. However, this can be cost-prohibitive for many patients as medical cannabis is not covered by insurance so trialing several different products to find the right fit might not be feasible in the general population.

CLINICAL PEARL: It is hard to generalize study findings examining medical cannabis for symptom management given the variability of strains and components in each product.