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:

Cannabis Hyperemesis Syndrome

Background:

In 2016, the Medical Marijuana Program paved the way for use of medical cannabis in Pennsylvania for patients suffering from cancer, severe chronic or intractable pain, and terminal illness. (of note: despite being approved for use in 18 states, cannabis is federally still considered a Schedule I drug) Given the increase use of cannabis for symptomatic relief in our palliative care population, it is important to recognize the associated adverse effects. Cannabis hyperemesis syndrome (CHS) is characterized by cyclic episodes of nausea and vomiting (N/V) due to chronic cannabis use. While the exact cause of CHS is unknown, there are three hypothesized mechanisms. The cannabinoid receptors 1 (CB1) located in the gastrointestinal tract may reduce gastric emptying causing N/V. The second hypothesis examines he lipid soluble property of THC. During stress when fat is broken down, it may lead to a large release of THC build up causing a "re-intoxication effect". Lastly, genetic P450 polymorphisms may affect rate at which THC is metabolized in the liver. Given the uncertainty regarding mechanism of CHS, treatment options are variable.

Importance:

Given the increased use of medical cannabis (generally speaking), it is important for palliative care clinicians to understand the data surrounding treatment of potential adverse effects associated with chronic cannabis use.

The Literature:

Med Princ Pract. 2021 Nov 1. doi: 10.1159/000520417

A Systematic Review on Cannabis Hyperemesis Syndrome and Its Management Options

Methods:

- Literature review from January 2009 to June 2021 that describes the use of cannabinoids and CHS in adults and older population
- N=17 articles included, 9 case reports, 2 RCT, 2 retrospective cohort studies, and 4 systematic reviews

Objectives:

- Highlight current management options for CHS

Results:

- In all studies, discontinuation of cannabinoid was the best method to alleviate symptoms
- Topical capsaicin provided short-term relief – RCT comparing 0.1% capsaicin vs. placebo found 46% vs. 24.9% reduction respectively in nausea based on the visual analog scale (VAS) 60 minutes after administration
- Droperidol administration resulted in shorter length of stay, decreased necessity of other antiemetics and showed significant decrease in VAS nausea severity
- Case reports and one RCT showed benefit of haloperidol for CHS (see below for RCT)
- Limited evidence for hot water hydrotherapy, propranolol, benzodiazepine, and aprepitant for CHS

Conclusion: Some nonconventional pharmacological strategies may be helpful for CHS management, although limited evidence exists

Ann Emerg Med. 2021 Jun;77(6):613-619.

Intravenous Haloperidol vs. Ondansetron for Cannabis Hyperemesis Syndrome: A Randomized Controlled Trial

*this study was included in the literature review above

Methods: RCT, triple blinded, crossover trial comparing ondansetron 8mg IV, low dose (0.05 mg/kg) haloperidol, and higher dose (0.1 mg/kg) haloperidol in the emergency department

- **Exclusion: patients taking daily opioids**

Outcomes:

- Primary: average change in visual analog score (0-10) for abdominal pain and nausea at baseline vs. two-hours after administration
- Secondary: changes in either abdominal pain or nausea score over time, treatment success, discharge ready at two hours, use of rescue antiemetics before discharge, time to discharge, readiness, length of stay greater than 12 hours, and unscheduled return visits within 7-days
- Safety: any adverse effects potentially related to study drug (ie: dystonia, akathisia)

Results: n = 30 (received at least one treatment) average age: 29 years; 1.5-gram daily average consumption of cannabis for ~10 years

- Haloperidol group saw a larger reduction in abdominal pain and nausea compared to ondansetron (mean difference of 2.3 cm on VAS (95% CI 0.6 to 4.0 cm *p=0.01*)
- Use of haloperidol was associated the following (combined both dosing groups for haloperidol for outcomes given small N):
  - Higher treatment success: 54% vs. 29% (24% difference (95% CI – 16% to 59%))
  - Reduced use of rescue antiemetics: 31% vs. 59% (28% difference (95% CI – 61% to 13%))
  - Shorter time to discharge: 3.1 hours (SD 1.7) vs. 5.6 (SD 4.5) (2.5 hr difference (95% CI 0.1 – 5 hour) P=0.03)
- Reports of one moderate akathisia and two return visits for acute dystonia after higher dose of haloperidol
- Average dose of haloperidol administered: 3.7mg – 7.35mg (calculated from average weight of participants in haloperidol group of 73.4kg and dosing range of 0.05mg/kg-0.1mg/kg)

Conclusion:

- Low-dose IV haloperidol was found to be beneficial in management of active nausea and vomiting due to cannabis hyperemesis compared to ondansetron in the emergency department

Bottom Line:

- The most reliable management strategy for CHS is to stop the use of cannabis, although this may be an unfavorable option for our patients if using for symptomatic relief (although our patients are likely utilizing lower doses, been on cannabis for a shorter period, and at lower risk for CHS in general)
- While there are multiple possible management strategies, there is a lack of evidence to make a strong case for one pharmacologic agent over another
- To note, the RCT trial comparing haloperidol and ondansetron excluded patients on daily opioids which would exclude many of our palliative care patients, so this makes us question how applicable this study is to our patients..? Would being on opioids alter the results…?
- Interesting weight-based dosing utilized in the RCT… if using haloperidol for CHS, caution should be advised for acute dystonia in higher doses (0.1 mg/kg, ~7mg)

CLINICAL PEARL: CHS may be palliated with nontraditional pharmacologic agents, although discontinuing cannabis is the most promising "treatment" of all.