Pharmacy Friday

Brief pearls related to acute care pharmacology and evidence-based medicine
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Cannabinoid Hyperemesis Syndrome (CHS)

Introduction

1. Commonly identified as symptoms, including nausea, cyclic vomiting and abdominal pain, that are refractory to available antiemetics and analgesics.

2. Patients tend to take compulsive hot baths/showers for symptom relief.

3. Characteristically distinguished from cyclic vomiting syndrome, these symptoms are usually preceded by years of chronic cannabis use and symptoms are typically resolved with cessation of cannabis use

4. Patients often present with severe abdominal pain. Opioids should be avoided for analgesic pain if CHS is suspected as it may induce/worsen nausea and vomiting symptoms

Pharmacology			
	Capsaicin	**Haloperidol**	**Benzodiazepines**
Mechanism	Hot water stimulates a G-protein coupled receptor on peripheral tissue, transient receptor potential vanilloid-1 ($TRPV_1$), that interacts with endocannabinoid system causing relief of nausea and vomiting. This is the only known capsaicin receptor.	Postsynaptic dopaminergic blockade at D_2 receptors in the gastrointestinal tract and the chemoreceptor trigger zone	Stimulation of inhibitory neurotransmitter gamma-aminobutyric acid (GABA) to reduce anticipation of nausea and vomiting. Additionally, decreased activation of the cannabinoid type receptor 1 (CB1) receptor in the frontal cortex.
Dose	0.075%: 3-4 times per day	1-5mg Doses from 1 - 2.5mg are often enough for symptom improvement and should be tried first	Clonazepam 0.5mg *other benzos are likely appropriate too
Administration	Topical application to abdomen or back of arms (prioritize treatment to a certain area in which hot water provides symptom relief	IV, PO	PO, ODT
Formulations (recommended for use)	Topical Cream 0.075%	IV, PO	PO, ODT
Adverse Effects	Burning/uncomfortable on skin on initial application	Extrapyramidal reaction (low risk)	Drowsiness, confusion, respiratory depression
Drug Interactions and warnings	Burns and CNS depression are possible Avoid touching eyes mouth and genitals	Caution use in psychiatric disorders QT prolonging agent	Caution in hepatic/renal dysfunction
	THE ONLY CURRENT DEFINITIVE TREATMENT IS CESSATION OF CANNABIS USE **Standard of care prophylaxis and treatment of nausea/vomiting should be provided prior to ruling ineffective and moving on to above therapies**		

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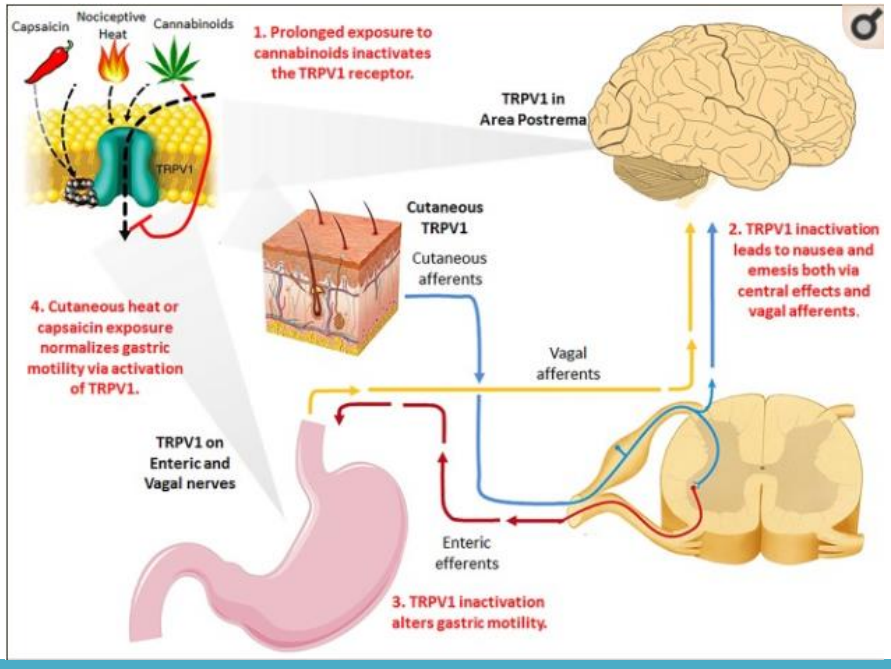

Overview of Evidence			
Author, year	**Design/ sample size**	**Intervention & Comparison**	**Outcome**
Inayat 2016	Case Report N =1	• Haloperidol 1-2mg IV	No relief of symptoms at 2 days with ondansetron, lorazepam and IV hydration. Patient responded to **1mg IV haloperidol** with decreased gastrointestinal symptoms and compulsive hot bathing. **Subsequent doses of 2mg** were given.
Jones 2016	Case Report N=1	• Haloperidol 5mg PO daily	Treated in the outpatient setting with **oral haloperidol 5mg daily**. Symptom relief was reported after 1 day of haloperidol use. Patient self-discontinued after 3 weeks without recurrence of symptoms but unable to determine how long this effect lasted due to patient being lost to follow up
Witsil 2017	Case Series N=4	• Haloperidol 5mg IV	All 4 patients failed standard of care therapy. All were given a dose of **haloperidol 5mg IV** with reported resolution of nausea and vomiting within 1-2 hours.
Dezieck 2017	Case series N=13	• Topical Capsaicin	All 13 patients, who used cannabis daily, experienced relief of symptoms with **topical capsaicin cream in the emergency department** when other standard treatments failed to provide relief from nausea/vomiting
Moon 2018	Case Report N =1	• Topical Capsaicin 0.075%	Failed treatment of: ondansetron, metoclopramide, and prochlorperazine. **0.075% capsaicin cream applied to periumbilical region, repeated every 4 hours.** Complete resolution of symptoms was seen after 3 doses.
Kheifets 2019	Case Series N=4	• Clonazepam 0.5mg PO q8h	All 4 patients were refractory to conventional IV antiemetics. 2 patients used cannabis chronically on a weekly basis and 2 patients on a daily basis. Patients were treated with **clonazepam 0.5mg PO q8h**. 2 patients had symptom relief after 1 dose and 2 patients within 24 hours.
In the works HaVOC trial	Prospective N= estimate 80	• Haloperidol 0.05mg/kg IV • Haloperidol 0.1mg/kg IV • Ondansetron 8mg IV	Results pending

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