Pharmacotherapy for Management of Cannabinoid Hyperemesis Syndrome (CHS)

Introduction

- CHS is a syndrome of cyclic vomiting, nausea, and abdominal pain often refractory to available antiemetics and analgesics in patients who chronically use cannabis.
    - Hallmark symptom of CHS is compulsive hot bathing as it results in symptom relief.
- **Cannabis cessation is the only current definitive treatment of CHS.**
    - Treatment is unknown, but regimens include capsaicin, dopamine antagonists, and benzodiazepines.
    - Opioids should be avoided as they may exacerbate nausea and vomiting.

Pharmacology			
	Capsaicin	**Dopamine Antagonists**	**Benzodiazepines**
Mechanism of Action	Stimulates transient receptor potential vanilloid-1 (TRPV1), a G-protein coupled receptor on peripheral tissue; TRPV1 interacts with the endocannabinoid system resulting in symptom relief	Antagonizes dopamine receptor upregulation in chronic cannabis use; targets D2 receptors in the gastrointestinal tract and chemoreceptor trigger zone	Stimulation of inhibitory neurotransmitter GABA to reduce nausea/vomiting anticipation; dereases activation of cananbnioid type receptor 1 (CB1) in frontal cortex
Dose	2-3 inch strip	Haloperidol: 1-5 mg Droperidol: 0.625-2.5 mg	Clonazepam: 0.5 mg
Administration	Topical application to abdomen or back of arms	IV, PO	IV, PO, ODT
Recommended Dosage Form	Cream: 0.05%, 0.075%, 0.1%	IV	IV, ODT
Adverse Effects	Burning & itching	Extrapyramidal reactions	Drowsiness, confusion, respiratory depression
Drug Interactions & Warnings	Avoid touching eyes, mouth & genitals after application; should be applied wearing gloves *8% patch utliziation may result in severe skin irritation/burns	Caution use in psychiatric disorders; QT prolonging agent	Caution in hepatic and/or renal dysfunction

Sam Wagner & Jimmy Pruitt; Jimmy@pharmacyfridaypearls.com

Overview of Evidence			
Author, Year	**Design (Sample Size)**	**Intervention & Comparison**	**Outcomes**
		Capsaicin	
Kum et al., 2021	Retrospective, cohort (n=201)	Topical capsaicin Adult & pediatric patients	• Greater proportion of patients who received capsaicin achieved primary efficacy outcome (55 vs 21%, p<0.001, OR 1.44 [95% CI 0.586-0.820]) • Reduction in time to discharge following capsaicin admin (3.72 vs 6.11 hr, p=0.001)
Yusuf et al., 2021	Retrospective, observational (n=55)	Topical capsaicin vs no capsaicin	• Capsaicin administration within first two rounds of medication treatment had significantly shorter length of stay (4.83 vs 7.09 h, p=0.01) • No difference in 24 h bounceback or admission rate between groups (0.11 vs 0.10, p=0.43; 0.19 vs 0.05, p=0.07)
Dean et al., 2020	Double-blind, randomized, placebo-controlled (n=30)	Topical capsaicin 0.1% vs placebo	Capsaicin administration was associated with significant reduction in nausea/vomiting at 30 and 60 minutes by visual analog scale (difference -2, 95% CI 0.2 to -4.2; difference -3.2, 95% CI -0.9 to -5.4)
Wagner et al., 2020	Retrospective, matched cohort (n=43)	Topical capsaicin (varying strengths) vs no capsaicin	• Trend towards reduction in ED length of stay with capsaicin use (179 vs 201 min; p=0.33) • 67% of patients did not require any additional rescue medications prior to discharge
Graham et al., 2018	Case series (n=2)	Topical capsaicin 0.025% Adolescent patients	Following failure of other medications, both patients reported symptom relief within 30 minutes following capsaicin administration
Dezieck et al., 2017	Multicenter case series (n=13)	Topical capsaicin (varying strengths)	All patients reported symptom relief following capsaicin administration though several required additional rescue medications
		Dopamine Antagonists	
Ruberto et al., 2021	Randomized. Controlled (n=33)	Haloperidol 0.05 mg/kg IV Haloperidol 0.1 mg/kg IV Ondansetron 8 mg IV	• Haloperidol at either dose was superior to ondansetron (diff 2.3 on VAS, 95% CI 0.6-4) • Less use of rescue antiemetics in haloperidol group (31 vs 59%, 95% CI -61 to 13)
Lee et al., 2019	Retrospective, comparative (n=76)	Droperidol IV (avg dose 0.625 mg) vs no droperidol	• Length of stay was significantly lower in the droperidol group (6.7 vs 13.9 hours, p=0.014) • Ondansetron/metoclopramide use was reduced by half with the use of droperidol
Witsil et al., 2017	Case series (n=4)	Haloperidol 5 mg IV	All 4 patients reported resolution of nausea/vomiting within 1-2 hours of haloperidol administration
Inayat et al., 2016	Case report (n=1)	Haloperidol 1-2 mg IV	GI symptoms and compulsive hot bathing resolved with haloperidol 1 mg; subsequent symptoms resolved with haloperidol 2 mg
Hickey et al., 2013	Case report (n=1)	Haloperidol 5 mg IV	All CHS symptoms completely resolved within 1 hour of haloperidol administration
		Benzodiazepines	
Kheifets et al., 2019	Case series (n=4)	Clonazepam 0.5 mg PO q8h	2 patients had symptom relief after 1 dose, the remaining patients had symptom relief after 24 hours

Conclusions

- Capsaicin and dopamine antagonists appear as potential treatment options for CHS symptom management; however the only true treatment is cannabis cessation.

References

1. Lapoint J, et al. West J Emerg Med. 2018:19(2):380-86.
2. Sorensen CJ, et al. J Med Toxicol. 2017;13:71-87.
3. Kum, et al. Am J Emerg Med. 2021;49:343-51.
4. Yusuf, et al. Am J Emerg Med. 2021;43:142-8.
5. Dean, et al. Acad Emerg Med. 2020;27(11):1166-72.
6. Wagner S, et al. Clin Toxciol (Phila). 2020;58(6):471-5.
7. Graham, et al. Pediatrics. 2017;140(6):e20163795.
8. Dezieck L, et al. Clin Toxicol (Phila). 2017;55(8):908-13.
9. Ruberto A, et al. Ann Emerg Med. 2021;77(6):613-9.
10. Lee, et al. Clin Toxicol (Phila). 2019;57(9):773-7.
11. Witsil JC, et al. Am J Ther. 2017;24(1):e64-7.
12. Inayat F, et al. BMJ Case Rep. 2017;bcr2016218239.
13. Hickey JL, et al. Am J Emerg Med. 2013;31(6):1003.e5-6.
14. Kheifets M, et al. IMAJ. 2019;21:404-7.