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# 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 | | | |
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| | **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<br>Droperidol: | 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<br><br>*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 |

| Overview of Evidence | | | |
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| **Author, Year** | **Design (Sample Size)** | **Intervention & Comparison** | **Outcomes** |
| ***Capsaicin*** | | | |
| Kum et al., 2021 | Retrospective, cohort (n=201) | Topical capsaicin<br>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]) |

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| | | | • 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)<br>• 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)<br>• 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<br>Haloperidol 0.1 mg/kg IV<br>Ondansetron 8 mg IV | • Haloperidol at either dose was superior to ondansetron (diff 2.3 on VAS, 95% CI 0.6-4)<br>• 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)<br>• 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.


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