Haloperidol as a treatment option in cannabinoid hyperemesis syndrome

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A review of the current medical literature recognizes cannabinoid hyperemesis syndrome (CHS) as recurrent episodes of heavy nausea and vomiting with clinical stability and symptomatic resolution between episodes [1]. A prerequisite for CHS is the use of cannabis or cannabinoid-containing products. Two distinct phases make up CHS: a long prodromal phase (often lasting several years) with chronic bouts of nausea, abdominal pain, and fear of vomiting, and an active intractable hyperemetic phase [1]. During the hyperemetic phase of CHS, patients present acutely in a hospital setting and are discharged after empiric treatment with antiemetic medications. Patients find themselves with acute symptom relapse and have multiple hospital admissions with similar presentations. From the current literature review, only in complete abstinence from cannabis or cannabinoid-containing products can patients have resolution of symptoms [1].

We present a unique treatment approach, exploring the use of haloperidol as an effective treatment for a severe case of CHS.

A previously healthy 20-year-old black woman arrived at the emergency department (ED) with a 3-day history of nausea associated with multiple episodes of intractable non-bilious, non-bloody vomiting, accompanied by severe diffuse abdominal cramping. She had previously been hospitalized 7 times for this presentation and had numerous unremarkable diagnostic tests. The patient admitted to previous episodes of cyclical vomiting that continue to occur every month and last up to several hours. The symptoms were not related to her menstrual cycle. This patient had no family history of such a disorder. The patient admitted to smoking marijuana several times daily for the last 8 years. She denied any concomitant alcohol use or history of eating disorder. Vital signs on admission were significant for a heart rate of 99 bpm and decreased blood pressure of 100/60 mm Hg. Blood work was remarkable for a mild reactive leukocytosis of (16.8×10^9/l) and notable for hypokalaemia of 3.0 mmol/l. All other laboratory investigations were unremarkable including COVID-19 testing, computed tomography (CT) of the abdomen and pelvis, stool occult blood, and *Helicobacter pylori* testing. The patient underwent upper endoscopy, which was also unremarkable. Despite acute management involving the administration of intravenous fluids, antiemetics, and prompt electrolyte repletion, the patient continued to experience intractable nausea and vomiting. The patient was then given haloperidol 5 mg IV for her intractable emesis, which resulted in symptomatic resolution of her nausea, vomiting, and abdominal pain within 1 h. Upon discharge the patient was instructed to continue close follow-up with her primary care physician and gastroenterologist. The patient was additionally referred to a community substance abuse clinic for further treatment. The patient remains abstinent from marijuana and has revealed symptomatic resolution following cannabis cessation at 6-week follow up.

CHS most typically presents in the acute hyperemetic stage, and it is often overlooked in the emergency department. Only after obtaining a detailed history of long-term cannabis use, cyclical vomiting, and compulsive hot water bathing does a clinician consider CHS as a possible diagnosis. CHS is made up of 3 phases: a prodromic, a hyperemetic, and a recovery phase [1]. The prodromal phase usually lasts months or even years, with most patients developing nausea, a persistent fear of vomiting, and abdominal pain. During this stage users end up relying on cannabis more to alleviate the effects of the nausea [1]. During the hyperemetic phase, patients present acutely with intractable nausea, vomiting, and retching. Patients often use hot water bathing as a last resort to achieve relief before presenting

to the ED. The reason this may be effective is due to the dose-dependent hypothermic effects of cannabinoids and their cross-regulation with the cannabinoid CB1-receptors in the hypothalamus, which regulates body temperature [2]. Patients present to the ED in this phase, which can lead to an unnecessary increase in healthcare costs through extensive workups including baseline labs like blood cell counts, blood glucose levels, liver function tests, imaging: abdominal X-ray, computerized tomography, and ultrasound, and procedures including esophagogastroduodenoscopy (EGD) and colonoscopy [3, 4].

Biochemically, tetrahydrocannabinol (THC) is the active ingredient in cannabis, it has been proposed that lipophilic properties and extended half-life may explain how CHS occurs when toxic levels accumulate [5]. The exact pathophysiology of CHS remains undetermined. It has been suggested that cannabinoids (CBs) cause slowing of enteric motility and chronic stimulation of cannabinoid 1 receptors (CB1Rs) leading to receptor downregulation, which may play a paradoxical role in increasing emesis in CHS [6].

The duration of time that the majority of cannabis users developed CHS was after 1 year of daily use, and the recurrence of cyclic vomiting was reported in 100% of these patients [7]. The demographic patient sub-population most likely to develop CHS were young adult males, with an average age of 24 years [7]. Given the significant difficulty in diagnosing patients with CHS there was a mean delay of symptom onset to diagnosis of 4 years [7].

Complete cessation of cannabinoid use has been identified as the only reliable treatment for CHS, based on a comprehensive literary review of CHS from January 2000 to September 2015 [8]. Optimal treatment for CHS may extend beyond empiric antiemetic therapy, with recent evidence that haloperidol is superior to ondansetron for the acute treatment of CHS. Patients treated with haloperidol achieved a significant reduction from baseline abdominal pain and nausea 2 h after treatment [9]. The role of haloperidol in the treatment of CHS can be explained by the crosstalk between dopamine 2 receptor (D2R) and CB1R, which explains why anti-dopaminergic receptor antagonists are of therapeutic value in treating the syndrome [9, 10].

In addition, it has been shown that haloperidol has been effective in the management of gastroparesis in the emergency department [11]. Some antiemetics such as metoclopramide, promethazine, and haloperidol are believed to antagonize D2 and D3 receptor in the medulla, which targets emesis provocation from the area postrema [11]. Based on the current literature, haloperidol may be the cornerstone drug in treating CHS patients who have failed to respond to other conservative management.

Although the direct mechanism responsible for the symptoms of intractable nausea and vomiting is still unclear, haloperidol is an effective method of treatment for the hyperemetic phase of CHS and can be used as an adjunct to empiric antiemetic therapy. The most reliable treatment for CHS is complete cessation of cannabinoids. Further research is needed to understand the underlying pathophysiology of CHS with a special focus on haloperidol to reduce hospital admissions and length of stay.

Conflict of interest

The authors declare no conflict of interest.

References

1. Sun S, Zimmermann AE. Cannabinoid hyperemesis syndrome. Hosp Pharm 2013; 48: 650-5.
2. Chang YH, Windish DM. Cannabinoid hyperemesis relieved by compulsive bathing. Mayo Clin Proc 2009; 84: 76-8.
3. Wallace EA, Andrews SE, Garmany CL, et al. Cannabinoid hyperemesis syndrome: literature review and proposed diagnosis and treatment algorithm. South Med J 2011; 104: 659-64.
4. Sontineni SP, Chaudhary S, Sontineni V, Lanspa SJ. Cannabinoid hyperemesis syndrome: clinical diagnosis of an underrecognised manifestation of chronic cannabis abuse. World J Gastroenterol 2009; 15: 1264-6.
5. Allen JH, de Moore GM, Heddle R, Twartz JC. Cannabinoid hyperemesis: cyclical hyperemesis in association with chronic cannabis abuse. Gut 2004; 53: 1566-70.
6. Inayat F, Virk HUH, Ullah W, Hussain Q. Is haloperidol the wonder drug for cannabinoid hyperemesis syndrome? BMJ Case Rep 2017; 2017: bcr2016218239.
7. Bajgoric S, Samra K, Chandrapalan S, Gautam N. Cannabinoid hyperemesis syndrome: a guide for the practising clinician. BMJ Case Rep 2015; 2015: bcr2015210246.
8. Sorensen CJ, DeSanto K, Borgelt L, et al. Cannabinoid hyperemesis syndrome: diagnosis, pathophysiology, and treatment – a systematic review. J Med Toxicol 2017; 13: 1-87.
9. Ruberto AJ, Sivilotti MLA, Forrester S, et al. Intravenous haloperidol versus ondansetron for cannabis hyperemesis syndrome (HaVOC): a randomized, controlled trial. Ann Emerg Med 2021; 77: 613-9.
10. Chiang YC, Lo YN, Chen JC. Crosstalk between dopamine D2 receptors and cannabinoid CB1 receptors regulates CNR1 promoter activity via ERK1/2 signaling. J Neurochem 2013; 127: 163-76.
11. Ramirez R, Stalcup P, Croft B, Darracq MA. Haloperidol undermining gastroparesis symptoms (HUGS) in the emergency department. Am J Emerg Med 2017; 35: 1118-20.

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