CASE REPORT

Is haloperidol the wonder drug for cannabinoid hyperemesis syndrome?

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Accepted 10 December 2016

SUMMARY

Cannabinoid hyperemesis syndrome (CHS) is a rare clinical syndrome characterised by nausea, cyclic vomiting and severe abdominal pain in association with chronic cannabis use. It is often under-recognised or misdiagnosed, resulting in the unnecessary workup and frequent hospitalisations. Long-term treatment of CHS is abstinence from cannabis, but acute symptomatic management has been a struggle for many clinicians. The present report highlights the use of haloperidol as an agent that successfully and safely treats the unrelenting symptoms of CHS.

BACKGROUND

Cannabinoid hyperemesis syndrome (CHS) is a recently described clinical condition that has frequently been associated with marijuana use. Clinicians should maintain a high index of suspicion for CHS in patients presenting with cyclical nausea and vomiting, especially when there is a history of compulsive hot showers and cannabis use. Regarding the management of CHS, there is no definitive pharmacological therapy to employ in the emergency department. Haloperidol is often used as an antiemetic; however, it has rarely been administered in patients with CHS. The present patient was a non-responder to conservative management but demonstrated a striking response to haloperidol.

CASE PRESENTATION

A 27-year-old man with a history of marijuana abuse presented to the emergency department with nausea, vomiting and abdominal pain for 3 days. The patient reported 15–20 episodes of non-bloody, non-projectile and non-bilious vomiting. These episodes were associated with diffuse, non-radiating and colicky abdominal pain alleviated partially by taking hot showers. He also noticed foul-smelling soft stools. The patient reported of having intermittent episodes of stomach upset with intractable vomiting after marijuana use for 2 years, which got better after hot baths. He has been hospitalised multiple times following the same symptoms in association with the cannabis use. However, in his current presentation, the symptoms were more severe. The patient denied fever, chills, unusual eating behaviour, sick contacts, haematemesis, melena, haematochezia or recent travel.

On physical examination, his vital signs were normal. Abdominal examination revealed a soft, non-tender and non-distended abdomen. There was no rebound or tenderness and bowel sounds were normal. Initial laboratory evaluation was unremarkable. Biochemical tests were negative for electrolytes and acid–base abnormalities. Hepatic and pancreatic enzymes were within normal limits. The patient reported active use of marijuana for past ~10 years; smoked at least five joints a day.

INVESTIGATIONS

On admission, the toxicology screening came out positive for cannabis. In view of our patient's cyclic vomiting pattern, and repetitive admissions; extensive workup was conducted to exclude other causes of these alarming signs and symptoms. CT of the abdomen and MRI of the brain were normal. Upper endoscopy and colonoscopy were also non-significant. A gastric emptying study was also unremarkable. On the basis of long-term cannabis use, severe cyclic nausea and vomiting, abdominal pain, resolution of symptoms with cannabis cessation, temporary relief of symptoms with hot showers, age younger than 50 years, and negative findings on diagnostic evaluation; our patient was diagnosed with CHS.

TREATMENT

The patient was initiated on ondansetron and intravenous hydration. However, severe hyperemesis persisted even after 2 days of conventional antiemetic treatment. During the hospitalisation, he continued taking hot showers that transiently alleviated his symptoms. There, the treatment was attempted with lorazepam; however, there was no relief. Subsequently, after obtaining informed consent from the patient, it was decided to give a trial of haloperidol. He was initially administered 1 mg intravenous haloperidol (Haldol, Janssen Pharmaceuticals, Raritan, New Jersey, USA). The patient responded well to the treatment with a clinically significant improvement without any adverse reactions. His compulsive hot bathing and the gastrointestinal symptoms began to diminish following next two dosages of 2 mg intravenous haloperidol.

OUTCOME AND FOLLOW-UP

On day 3 of admission, the patient started tolerating regular oral intake demonstrating an unremarkable recovery after total three doses of intravenous haloperidol. He was discharged from the hospital with strong counselling for permanent cannabis cessation. At the 1-month follow-up visit, he did not report recurrence of nausea, vomiting or abdominal pain. Since then, the patient continues to enjoy a stable and healthy life.

To cite: Inayat F, Virk HUH, Ullah W, *et al*. *BMJ Case Rep* Published online: [*please include* Day Month Year] doi:10.1136/bcr-2016-218239

DISCUSSION

Cannabis is the most commonly used illicit drug in the USA.[1 2] Although it has documented medicinal benefits as an antiemetic, chronic cannabis use has recently been linked to CHS. The exact pathophysiology of this phenomenon remains undetermined, but few theories exist in the medical literature. It is believed that chronic stimulation of cannabinoid 1 (CB1) receptors causes CHS by receptors' downregulation leading to cyclic nausea and vomiting.[3 4] Furthermore, CBs have been shown to slow enteric motility and chronic, high-dose exposure may increase the decelerating effects on the gut and supersede the antiemetic effects in the brain.[3] These, however, do not explain the compulsive hot bathing and showering in patients with CHS.

Previously, it has been speculated that hot baths help to relieve CHS symptoms by increasing body temperature and potentially reversing the chronic hypothalamic CB receptor stimulation that may have caused CHS-related nausea, vomiting and abdominal pain.[5] Another theory highlighted potential causation of CHS secondary to enteric CB receptor-mediated vasodilation in the gut and hot showers may have a role in relieving cyclic nausea and vomiting in these patients by diverting blood to the periphery.[5 6] However, there is not much evidence to support these theories and it is a matter of meticulous research.

CHS poses a significant diagnostic challenge owing to its nonspecific gastrointestinal symptoms. Physicians at Mayo Clinic, Rochester, Minnesota, USA, proposed a set of major and supportive clinical characteristics to diagnose CHS.[7] The long-term cannabis abuse was deemed as the single most important feature for diagnosis. Other than that, the major characteristics included severe cyclic nausea and vomiting, abdominal pain, resolution of disease after cannabis cessation, and relief of CHS symptoms with hot showers. Supportive features included weight loss of >5 kg, age <50, disease symptoms more pronounced in the morning, no change in bowel habits and exclusion of other probable aetiologies. However, it should be noted that not all cannabis users develop these symptoms indicating the possibility that patients with CHS may have an increased sensitivity towards cannabis. Our patient fits the diagnostic criteria because of his chronic cannabis abuse, consistent clinical presentation and partial relief of symptoms after hot water baths.

Management of CHS has largely been a predicament due to its unclear pathogenesis. It is mainly supportive and educational. While patients with CHS commonly use hot showers and baths to temporarily combat debilitating symptoms, cannabis cessation is the only definitive treatment thus for.[3] When these patients present to the emergency department, the major goals of acute treatment consist of managing abdominal pain, prevention of vomiting, and correction of fluid and electrolyte imbalance. A number of antiemetic drugs, such as D2 and H1 receptor antagonists, have been used with no obvious benefits. Interestingly, the present patient was refractory to the conventional antiemetic medications but showed remarkable response to haloperidol resulting in dramatic resolution of the cyclic vomiting and abdominal pain.

Haloperidol is an antipsychotic drug primarily used in the treatment of schizophrenia and other psychoses. In addition to its antipsychotic properties, it is a potent antiemetic. Anaesthesia literature has demonstrated the efficacy of haloperidol in postoperative nausea and vomiting possibly through its action on D2 receptors in the chemoreceptor trigger zone.[8 9] However, medical literature to support haloperidol as a standard therapy for CHS is scant. We conducted a comprehensive search of the PubMed database and reviewed the relevant papers published until September 2016, and found only three reports employing haloperidol as a successful therapy in patients with symptomatic CHS.[10–12]

CHS cases treated with haloperidol were all reported from the USA. These patients described in these case reports were below the age of 40 years and presented with nausea and intractable vomiting with a history of chronic cannabis abuse. It is important to note that CHS symptoms in all of these cases were refractory to repeated doses of conventional antiemetics. This highlights the importance of haloperidol as a novel therapy in such patients. The exact mechanism of how haloperidol works in CHS is unknown; however, the complex interaction between dopamine and CB1 signalling pathway is hypothesised to be responsible for the remarkable response in these patients.[13 14] To further show the therapeutic role of haloperidol, large clinical trials are warranted in patients presenting with CHS symptoms.

Learning points

- Cannabinoid hyperemesis syndrome (CHS) often results in repeated hospital admissions due to lack of definitive therapy. Although cannabinoid cessation is the only known way to prevent recurrence of this disease, prompt diagnosis and efficient symptom management could help to avoid unnecessary investigations and to decrease the rate of hospital admission in these patients.
- Haloperidol may be considered as an effective treatment option for patients with refractory CHS in the emergency department.
- The action of haloperidol at the cannabinoid 1 receptors suggests a possible mechanism for its beneficial effects in managing nausea and vomiting in CHS.
- Further clinical studies are required to broaden the scope of our knowledge on this issue and to frame guidelines to standardise the care of patients with CHS.

Acknowledgements The authors acknowledge Dr Abu Hurairah MD for his valuable input in the literature review and case management.

Contributors FI and WU did literature search and QH and HUHV wrote case presentation and summary.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

1 Bajgoric S, Samra K, Chandrapalan S, *et al*. Cannabinoid hyperemesis syndrome: a guide for the practicing clinician. *BMJ Case Rep* 2015;2015:pii: bcr2015210246.
2 Degenhardt L, Chiu WT, Sampson N, *et al*. Toward a global view of alcohol, tobacco, cannabis, and cocaine use: findings from the WHO World Mental Health Surveys. *PLoS Med* 2008;5:e141.
3 Patterson DA, Smith E, Monahan M, *et al*. Cannabinoid hyperemesis and compulsive bathing: a case series and paradoxical pathophysiological explanation. *J Am Board Fam Med* 2010;23:790–3.
4 Hopkins CY, Gilchrist BL. A case of cannabinoid hyperemesis syndrome caused by synthetic cannabinoids. *J Emerg Med* 2013;45:544–6.
5 Lu ML, Agito MD. Cannabinoid hyperemesis syndrome: marijuana is both antiemetic and proemetic. *Cleve Clin J Med* 2015;82:429–34.
6 Iacopetti CL, Packer CD. Cannabinoid hyperemesis syndrome: a case report and review of pathophysiology. *Clin Med Res* 2014;12:65–7.
7 Simonetto DA, Oxentenko AS, Herman ML, *et al*. Cannabinoid hyperemesis: a case series of 98 patients. *Mayo Clin Proc* 2012;87:114–9.

8 Gan TJ, Meyer T, Apfel CC, *et al*. Consensus guidelines for managing postoperative nausea and vomiting. *Anesth Analg* 2003;97:62–71.
9 Juurlink DN. Antipsychotics. In: Nelson LS, Lewin NA, Howland MA, Hoffman RS, Goldfrank LR, Flomenbaum NE, eds. *Goldfrank's toxicologic emergencies*. 9th edn. Ch. 69. New York: McGraw Hill, 2011:1003–15.
10 Hickey JL, Witsil JC, Mycyk MB. Haloperidol for treatment of cannabinoid hyperemesis syndrome. *Am J Emerg Med* 2013;31:1003.e5–6.
11 Witsil JC, Mycyk MB. Haloperidol, a novel treatment for cannabinoid hyperemesis syndrome. *Am J Ther* 2014;10:1097.
12 Jones JL, Abernathy KE. Successful treatment of suspected cannabinoid hyperemesis syndrome using haloperidol in the outpatient setting. *Case Rep Psychiatry* 2016;2016:3614053.
13 Schulze DR, Carroll FI, McMahon LR. Interactions between dopamine transporter and cannabinoid receptor ligands in rhesus monkeys. *Psychopharmacology (Berl)* 2012;222:425–38.
14 Desai RI, Thakur GA, Vemuri VK, *et al*. Analysis of tolerance and behavioral/physical dependence during chronic CB1 agonist treatment: effects of CB1 agonists, antagonists, and noncannabinoid drugs. *J Pharmacol Exp Ther* 2013;344:319–28.