RCEM best practice guideline: suspected cannabinoid hyperemesis syndrome in emergency departments

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ABSTRACT

Cannabinoid hyperemesis syndrome (CHS) is an episodic syndrome of cyclic vomiting in the context of the prolonged use of cannabis. The Royal College of Emergency Medicine Toxicology Special Interest Group has produced guidance to support emergency medicine clinicians with the recognition and treatment of people experiencing CHS.

Considerations regarding recognition, investigation and communication are discussed, and recommendations regarding treatment options (which include haloperidol and capsaicin) are made. There is a focus on making recommendations on the best available evidence.

PREFACE

The Royal College of Emergency Medicine best practice guideline (BPG) was produced by members of the Toxicology Special Interest Group. BPGs use a multimodal search strategy to produce guidance for areas of clinical controversy where little robust evidence exists or areas of particular concern or anxiety to Fellows and Members.[1] This BPG was originally published online in June 2023. There have been several limited changes made to reflect updates in the literature since the original publication.

KEY RECOMMENDATIONS

1. A diagnosis of cannabinoid hyperemesis syndrome (CHS) should be considered in presentations of nausea and vomiting with a cyclic pattern and where there is associated cannabis use. (Recommendation level C).
2. Patients should be encouraged to disclose their cannabis use and be reassured that this disclosure will not affect them adversely and will remain confidential. Care should be taken to ensure that patients do not feel stigmatised for their use of cannabis. (Recommendation level C).
3. Failure of standard antiemetic therapy to improve symptoms should lead to consideration of the use of haloperidol or capsaicin. (Recommendation level B).
4. Patients may struggle to accept a diagnosis of CHS for a variety of reasons. They should be supported with written information when a diagnosis of suspected CHS is made. This information should also identify sources of support and advice for helping those cannabis users wishing to achieve abstinence. (Recommendation level C).

A key to the Strength of Recommendations Taxonomy is given in table 1.

SCOPE

CHS is an episodic syndrome of cyclic vomiting in the context of the prolonged use of cannabis. It can be a challenging diagnosis to make, as vomiting episodes are not necessarily temporally related to increased cannabis use, and patients may find that cannabis use during an episode actually improves their symptoms. Identifying a relationship is made more difficult as patients may have weeks or months between episodes, and may develop the syndrome after many years of cannabis use. Identifying cannabis as the cause of symptoms may also be difficult due to patients' reluctance to disclose cannabis use.

It is important to recognise that CHS is unlikely to be definitively diagnosed in the ED due to the current diagnostic criteria. However, there are many clinical features which can lead clinicians to suspect a diagnosis of CHS and there are several non-conventional treatments that may be efficacious in treating the symptoms of CHS and may help to confirm it. The essential prerequisite for a CHS diagnosis is the long-term use of cannabinoids. There are no laboratory or radiographic investigations that can be used to diagnose CHS.

The process of creating this guideline has included contemporaneous literature reviews for high-level evidence in the medical literature on recognition and management of CHS, as well as searches for consensus agreement publications where they exist (PubMed search for 'cannabinoid hyperemesis' with all article types reviewed by title and abstract for relevance). The guideline group have formed consensus on areas lacking clear answers.

REASON FOR DEVELOPMENT

There are current gaps in accurately defining the optimal classification, pathophysiology and treatment of CHS. This BPG has been written to bridge the current gap between evidence and the need for emergency clinicians to provide quality care and advice to patients suffering from this syndrome.

Patients presenting with CHS often experience a delay to diagnosis. They will typically have repeated visits to EDs, several hospital admissions and often describe poor symptom control with standard therapies, such as antiemetic medications.

This guideline has been written to increase emergency medicine clinician awareness of CHS, support the care of patients presenting to the ED

Table 1 The Strength of Recommendations Taxonomy[26]

Strength of recommendation	Definition
A	Recommendation based on consistent and good quality patient-oriented evidence.
B	Recommendation based on inconsistent or limited quality patient-oriented evidence.
C	Recommendation based on consensus, usual practice, opinion, disease-oriented evidence and case series for studies of diagnosis, treatment, prevention or screening.

with symptoms of CHS and help clinicians communicate the concept and management of CHS to patients.

LIMITATIONS OF THE EVIDENCE

Since first being identified in 2004, CHS recognition has grown rapidly. However, leading systematic reviews remain at high risk of being impacted by publication bias, and clinical management is still in its infancy, with only small randomised controlled trials (RCTs) on which to base treatment advice.

BACKGROUND

7.8% of UK adults aged 16–59 years use cannabis, of whom 25.6% use cannabis at least weekly.[2]

While several mechanisms have been proposed, the exact pathophysiology of CHS is still unclear.[3] While cannabis can act as an antiemetic at low doses, repeated high dose use can result in vomiting. A clinical syndrome of hyperemesis in the context of cannabis use has been recognised as early as 2004. While overall recognition remains poor, recognition is improving.[4–6]

CHS is thought to be the cause of a significant proportion of presentations for recurrent vomiting and abdominal pain in EDs.[7] The diagnosis is frequently not considered, and the journey from onset to diagnosis can take an average of 4.1 years.[8] Patients may be reluctant to volunteer information about cannabis use in the ED unless reassured that they will not face legal consequences.

Patients are typically regular cannabis users, presenting with cyclic episodes of vomiting or abdominal pain. They often report relief of symptoms with hot showers or baths.

At its most severe, CHS can be fatal, but many other patients experience significant pain and distress, electrolyte abnormalities, hypoglycaemia or renal failure.[9] There is significant value in an early diagnosis for both treatment of the current episode, and prevention of future harm. Additionally, CHS often fails to resolve with standard antiemetic treatments. Some alternative therapies (which may not be routinely considered) have the potential to improve symptoms and avoid hospital admission.

RECOGNITION

The features in box 1 should prompt suspicion of a diagnosis of CHS.

Box 1 Frequency of features identified in diagnosis of cannabinoid hyperemesis syndrome[16]

⇒ Severe nausea and vomiting that recurs in a cyclic pattern over months (100%).
⇒ Age <50 years at time of evaluation (100%).
⇒ At least weekly cannabis use (97.4%).
⇒ Resolution of symptoms after cannabis cessation (96.8%).
⇒ Compulsive hot showers or baths with symptom relief (92.3%).
⇒ Abdominal pain (85.1%).
⇒ History of regular cannabis use for >1 year (74.8%).

The Rome IV diagnostic criteria for functional gastrointestinal disorders were defined in 2016.[10] One of the three criteria for definitive diagnosis of CHS is 'relief of vomiting episodes by sustained cessation of cannabis use', and therefore a confirmed diagnosis of CHS is unlikely to be made in an ED. Unfortunately, this criterion has limited the ability of researchers to definitively identify research populations in patients attending the ED.[11]

Consideration should also be given to re-evaluating previous diagnoses for recurrent vomiting disorders. One study identified that large numbers of patients with a diagnosis of cyclic vomiting syndrome were current cannabis users, although it is difficult to know if this represents management of cyclic vomiting syndrome symptoms with cannabis use, or a cohort of patients with undiagnosed CHS.[12]

Given the lack of specificity of many features of CHS, exclusion of a major medical or surgical aetiology as the cause for the patient's symptoms is essential. Potential other causes may include (but are not limited to):

- vomiting due to a central nervous system pathology;
- intra-abdominal pathology;
- infection, especially gastrointestinal;
- chronic nausea and vomiting syndrome;
- cyclical vomiting syndrome;
- diabetic gastroparesis.

INVESTIGATION

Complications of CHS are predominantly driven by poor food and fluid intake, and gastric losses due to intractable vomiting.

As well as following local policy for the investigation of abdominal pain and vomiting, specific consideration should be given to assessment for:

- hypoglycaemia;
- acute kidney injury;
- electrolyte abnormalities (sodium, potassium, calcium, chloride, magnesium);
- metabolic acidosis/alkalosis.

The presence of certain red flag signs or symptoms should alert clinicians to the possibility of an alternative diagnosis, such as:

- unintentional weight loss, especially aged >50 years;
- abdominal mass and/or change in bowel habit;
- anaemia or Liver Function Test abnormality.

COMMUNICATION

Clinicians should have sympathetic and non-judgemental discussions with the patient about their cannabis use, and recognise that patients may be nervous or reluctant to disclose their cannabis use. A variety of societal or health factors may lead to the use of cannabis, and harm from its use has been suggested to be lower than that of alcohol or tobacco.[13] Although there is limited data from RCTs, many patient advocacy groups have reported cannabis to be a helpful substance when standard therapies have failed.[14] Examples include Parkinson's disease, multiple sclerosis or chronic pain.

The role of cannabis in medicine is increasing, and some cannabis-based products are available on prescription in the UK.[15] Despite the number of current NHS prescriptions remaining low, it is recognised that thousands of private prescriptions have been issued.

Patients may struggle to accept the diagnosis of CHS for a variety of reasons:

- Vomiting episodes are not temporally related to an increase in cannabis use.
- Acute cannabis use often improves nausea.
- Patients may have weeks to months between episodes.
- Patients can develop the syndrome after using cannabis for <1 year or >11 years.[16]

Additionally, although it is easy to inform a patient they should stop using cannabis, cessation may be prove to be challenging.[17] Sign-posting advice, or referral to local services for help with drug use, may improve the likelihood of successful cessation.

It is recommended that written information on CHS be provided to patients. An example of such a leaflet is included with this guideline (online supplemental file 1).

SYMPTOM MANAGEMENT

Acute episode

CHS is recognised as often being resistant to routine antiemetic treatments such as cyclizine, dexamethasone, domperidone, metoclopramide, ondansetron, prochlorperazine and promethazine.[18 19] Additionally, pain relief with opiates is frequently unsuccessful.

Normal departmental processes for the management of nausea and vomiting should be followed in the first instance. A potential exception to this is a patient presenting with a known diagnosis of CHS and continued cannabis use.

Patients with an established diagnosis of CHS who have continued to use cannabis may present in the prodromal stage of an episode, with nausea, abdominal discomfort and fear of vomiting. Initiating treatment prior to vomiting may be helpful in this group.

Refractory symptoms

For refractory nausea or vomiting in CHS, consider the use of haloperidol or capsaicin, which are both supported by small RCTs and systematic reviews.[20–23] Suggested dosing is given in table 2.

Prior to administering haloperidol, obtain an ECG to check for QTc prolongation and correct any electrolyte abnormalities if conduction defects are present. Do not give haloperidol if the QTc is prolonged, or if a patient has Parkinson's disease or Lewy body dementia. Patients should be monitored for acute dystonia after administration. Do not discharge patients from the ED with a prescription for haloperidol unless this forms part of a specialty management plan.

If treatment fails to relieve symptoms and a patient requires admission, access to a hot shower or bath should be offered for symptom relief.

Other treatments, supported by extremely limited evidence (insufficient data to make dosing recommendations) include:

- benzodiazepines;
- droperidol;
- tricyclic antidepressants;
- olanzapine;
- levetiracetam;
- proton-pump inhibitors;
- beta-blockers.

Table 2 Treatment for refractory nausea and vomiting in cannabinoid hyperemesis syndrome

Medication	Route	Suggested dose
Haloperidol	Intramuscular*	0.05 mg/kg (maximum 5 mg)
Capsaicin 0.1% cream	Topical†	5 g of 0.1% cream applied to abdomen

*Although the trial used intravenous haloperidol, there is no UK intravenous licence. There is a UK licence for postoperative nausea and vomiting, although doses are lower.
†The evidence supports use of 0.1% cream, which does not have a UK license. 0.075% capsaicin (Axsain) is a licensed medication for neuropathic pain and postherpetic neuralgia and may be more easily sourced. However, there is insufficient evidence to make recommendations on the efficacy of this strength.

Long-term management

The only definitive treatment that has been identified to prevent CHS is abstinence from cannabis.

Special populations

Pregnancy—CHS may be mistaken for hyperemesis gravidarum, highlighting the need for a careful history-taking in such cases.[24]

Paediatrics—CHS has been described in adolescent patients. Paediatric patients may be exposed to cannabinoids through passive smoking or breast milk, although we were not able to find case reports linking these exposures to CHS.[25]

Review

Further review usually within 3 years or sooner if important information becomes available.

Disclaimers

The college recognises that patients, their situations, EDs and staff all vary. This guideline cannot cover all possible scenarios. The ultimate responsibility for the interpretation and application of this guideline, the use of current information and a patient's overall care and well-being resides with the treating clinician.

Research recommendations

Research is required to establish the prevalence of CHS in a UK setting, and optimal treatment strategies.

Audit standards

None.

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REFERENCES

1 Humphries C. 2024 Understanding RCEM best practice guidelines. *Emerg Med J*
2 Office for National Statistics. Available: https://www.ons.gov.uk/peoplepopulationandcommunity/crimeandjustice/datasets/drugmisuseinenglandandwalesappendixtable [Accessed 2 Nov 2022].
3 Perisetti A, Goyal H. Endocannabinoid system and Cannabis Hyperemesis syndrome: a narrative update. *Eur J Gastroenterol Hepatol* 2022;34:1–8.
4 Allen JH, de Moore GM, Heddle R, *et al*. Cannabinoid Hyperemesis: cyclical Hyperemesis in association with chronic Cannabis abuse. *Gut* 2004;53:1566–70.
5 Lua J, Olney L, Isles C. Cannabis Hyperemesis syndrome: still under recognised after all these years. *J R Coll Physicians Edinb* 2019;49:132–4.
6 Rotella JA, Ferretti OG, Raisi E, *et al*. Cannabinoid Hyperemesis syndrome: A 6-year audit of adult presentations to an urban district hospital. *Emerg Med Australas* 2022;34:578–83.
7 Simonetto DA, Oxentenko AS, Herman ML, *et al*. Cannabinoid Hyperemesis: a case series of 98 patients. *Mayo Clinic Proceedings* 2012;87:114–9.
8 Sorensen CJ, DeSanto K, Borgelt L, *et al*. Cannabinoid Hyperemesis syndrome: diagnosis, pathophysiology, and treatment—a systematic review. *J Med Toxicol* 2017;13:71–87.
9 Nourbakhsh M, Miller A, Gofton J, *et al*. Cannabinoid Hyperemesis syndrome: reports of fatal cases. *J Forensic Sci* 2019;64:270–4.
10 Stanghellini V, Chan FKL, Hasler WL, *et al*. Gastroduodenal disorders. *Gastroenterology* 2016;150:1380–92.
11 Bonnet U. Cannabis-related cyclic/episodic Hyperemesis conditions: from suspected to definitive Cannabinoid Hyperemesis syndrome. *Med Princ Pract* 2022;31:497–8.
12 Venkatesan T, Hillard CJ, Rein L, *et al*. Patterns of Cannabis use in patients with cyclic vomiting syndrome. *Clin Gastroenterol Hepatol* 2020;18:1082–90.
13 Nutt DJ, King LA, Phillips LD. Independent scientific Committee on drugs. drug harms in the UK: a Multicriteria decision analysis. *Lancet* 2010;376:1558–65.
14 Schlag AK, O'Sullivan SE, Zafar RR, *et al*. Current controversies in medical Cannabis: recent developments in human clinical applications and potential Therapeutics. *Neuropharmacology* 2021;191:.:S0028-3908(21)00140-4.
15 England NHS. Cannabis-based products for medicinal use, Available: https://www.england.nhs.uk/medicines-2/support-for-prescribers/cannabis-based-products-for-medicinal-use/ [Accessed 2 Nov 2022].
16 Sorensen CJ, DeSanto K, Borgelt L, *et al*. Cannabinoid Hyperemesis syndrome: diagnosis. *Pathophysiology, and Treatment-a Systematic Review J Med Toxicol* 2017;13:71–87.
17 Bonnet U, Preuss UW. The Cannabis withdrawal syndrome: Current insights. *Subst Abuse Rehabil* 2017;8:9–37.
18 Burillo-Putze G, Richards JR, Rodríguez-Jiménez C, *et al*. Pharmacological management of Cannabinoid Hyperemesis syndrome: an update of the clinical literature. *Expert Opinion on Pharmacotherapy* 2022;23:693–702.
19 Bhatt S, Queen J. Cannabinoid Hyperemesis syndrome. *Curr Emerg Hosp Med Rep* 2019;7:14–8.
20 Dean DJ, Sabagha N, Rose K, *et al*. A pilot trial of topical capsaicin cream for treatment of Cannabinoid Hyperemesis syndrome. *Acad Emerg Med* 2020;27:1166–72.
21 Ruberto AJ, Sivilotti MLA, Forrester S, *et al*. Intravenous haloperidol versus Ondansetron for Cannabis Hyperemesis syndrome (havoc): A randomized, controlled trial. *Annals of Emergency Medicine* 2021;77:613–9.
22 Senderovich H, Patel P, Jimenez Lopez B, *et al*. A systematic review on Cannabis Hyperemesis syndrome and its management options. *Med Princ Pract* 2022;31:29–38.
23 Pourmand A, Esmailian G, Mazer-Amirshahi M, *et al*. Topical capsaicin for the treatment of Cannabinoid Hyperemesis syndrome, a systematic review and meta-analysis. *The American Journal of Emergency Medicine* 2021;43:35–40.
24 Kirby J, Naren T. Cannabinoid Hyperemesis syndrome in pregnancy: challenges and opportunities. *Aust N Z J Obstet Gynaecol* 2023;63:746–52.
25 Lonsdale H, Kimsey KM, Brown JM, *et al*. Pediatric Cannabinoid Hyperemesis: A single institution 10-year case series. *J Adolesc Health* 2021;68:255–61.
26 Ebell MH, Siwek J, Weiss BD, *et al*. Strength of recommendation Taxonomy (SORT): A patient-centred approach to grading evidence in the medical literature. *Am Fam Physician* 2004;69:548–56.