The Royal College of Emergency Medicine

Best Practice Guideline

Suspected Cannabinoid Hyperemesis Syndrome in Emergency Departments

Royal College of Emergency Medicine

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Summary of Recommendations

1. A diagnosis of Cannabinoid Hyperemesis Syndrome (CHS) should be considered in presentations of nausea and vomiting with a cyclical pattern and where there is associated cannabis use.

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.

3. Failure of standard antiemetic therapy to improve symptoms should lead to consideration of the use of haloperidol or capsaicin.

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.

Scope

Cannabinoid Hyperemesis Syndrome (CHS) is an episodic syndrome of cyclical 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 Emergency Department (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 all aspects of CHS, as well as searches for consensus agreement publications where they exist. 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 best practice guideline 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 emergency departments, 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 with symptoms of CHS and help clinicians communicate the concept and management of CHS to patients.

Background

7.8% of UK adults age 16-59 use cannabis, of whom 25.6% use cannabis at least weekly.[1]

The pathophysiology of CHS is not clearly understood. 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, but overall recognition remains poor.[2,3]

CHS is thought to be the cause of a significant proportion of presentations for recurrent vomiting and abdominal pain in emergency departments (EDs).[4] The diagnosis is frequently not considered, and the journey from onset to diagnosis can take an average of 4.1 years.[5] Patients may be reluctant to volunteer information about cannabis use in the emergency department 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.[6] 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 Table 1 should prompt suspicion of a diagnosis of CHS.

• Severe nausea and vomiting that recurs in a cyclic pattern over months (100%)
• Age <50 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%)

Table 1. Frequency of features identified in diagnosis of CHS. Adapted from Sorensen *et al*.[7]

The Rome IV diagnostic criteria for functional gastrointestinal disorders were defined in 2016.[8] 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.[9]

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, though 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.[10]

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 age >50 years
- Abdominal mass and/or change in bowel habit
- Anaemia or LFT 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.[11] Although there is limited data from randomised controlled trials, many patient advocacy groups have reported cannabis to be a helpful substance when standard therapies have failed.[12] Examples include Parkinsons 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.[13] 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 less than 1 year, or greater than 11 years.[7]

Additionally, although it is easy to inform a patient they should stop using cannabis, cessation may be prove to be challenging.[14] 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 (Appendix 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.[15,16] 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.[17,18]

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

Table 2. Treatment for refractory nausea & vomiting in CHS.

(Although the trial used intravenous haloperidol, there is no UK intravenous licence. There is a UK licence for postoperative nausea and vomiting, though doses are lower*).**

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 (LBD). 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

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.

Paediatrics – CHS has been described in adolescent patients and exposure to cannabinoids may be through passive smoking.

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Review

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

Declaration of Interest

Christopher Humphries - Dept. of Health and Social Care Drug Harms Assessment and Response Team.

Marianne Gillings - nothing to declare.

Disclaimers

The College recognises that patients, their situations, Emergency Departments 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 wellbeing 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

Key words for search

Cannabinoid hyperemesis syndrome, cannabis hyperemesis, cannabis hyperemesis syndrome

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Appendix 1 – Example text for patient information factsheet

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Cannabinoid hyperemesis syndrome (CHS)
We have written this factsheet to give you more information about cannabinoid hyperemesis syndrome (CHS). It explains what cannabinoid hyperemesis syndrome is, the symptoms to look out for and how it is treated. We hope it will help to answer some of the questions you may have. If you have any further questions or concerns, please speak to a member of your healthcare team.

What is cannabinoid hyperemesis syndrome?
Cannabinoid hyperemesis syndrome (CHS) is a rare condition caused by a regular (daily) and long-term use of marijuana. The syndrome is characterised by repeated and severe bouts of vomiting.
Marijuana has several active substances. These substances bind to molecules found in the body and affect the way they work. For example, they affect the molecules found in the brain and cause the drug 'high' that users feel. They also affect the way the molecules in the gut function and can change the time it takes the stomach to empty. The drug also affects the oesophageal sphincter, which is the tight band of muscle that opens and closes to let food pass from the oesophagus (food pipe) into the stomach. The effects of marijuana on your digestive system are what lead to the main symptoms of CHS.

What causes CHS?
Marijuana is a complex substance that affects everyone differently. The main ingredient in marijuana is called THC, which has anti-nausea (anti-sickness) effects. This is why marijuana is regularly prescribed for nausea caused by chemotherapy treatment. However, if you use it over a long period of time, marijuana seems to have the opposite effect on the digestive system and makes you more likely to feel and be sick. Research is being carried out to explain why only some long-term users of marijuana experience CHS.

What are the symptoms?
Symptoms are divided into three stages:

1. **Prodromal phase**
   This is the first phase and symptoms may include early morning nausea, tummy (abdominal) pain and a fear of vomiting. During this phase, most people will keep to their normal eating patterns. Some people may continue to use marijuana because they think it will help stop the nausea. This phase may last for weeks, months or years.

2. **Hyperemetic phase**
   Symptoms may include:
   - ongoing nausea (feeling sick)
   - repeated episodes of vomiting
   - tummy pain
   - reduced food intake and weight loss
   - dehydration

   During this phase, vomiting may often be intense and overwhelming. Many people will take a lot of hot showers during the day to ease their nausea.

3. **Recovery phase**
   During this phase, the symptoms will go away and you will be able to eat normally again. This phase can last days or months. If you try marijuana again, your symptoms are likely to return.

When should I seek help?
Call your healthcare provider if you have had severe vomiting for a day or more, or are concerned that you may need medical treatment.

How is CHS diagnosed?
Many health problems can cause repeated vomiting. To make a diagnosis, your healthcare provider will ask you about your symptoms and your past health. They will also perform a physical exam, including an examination of your tummy. Your healthcare provider may also do further tests to rule out other causes of vomiting.
Disclosing to your healthcare provider that you use marijuana daily can speed up the diagnosis.

How is CHS treated?
If you have had severe vomiting, you may need to stay in hospital for a short time. During the hyperemesis phase, you may need the following treatments:

- IV (intravenous) fluid replacement for dehydration
- anti-sickness medicines
- pain-relief medicines
- proton-pump inhibitors (to treat stomach inflammation)
- frequent hot showers
- Capsaicin cream (to reduce pain and nausea)

Symptoms will often ease after a day or two, unless marijuana is used again. In order to fully recover, you will need to stop using marijuana all together. Some people may need support from drug rehabilitation programmes to achieve this. If you stop using marijuana, your symptoms should not come back.

What are the possible complications of CHS?
Very severe, prolonged vomiting may lead to dehydration. It may also lead to electrolyte problems in your blood. If left untreated, these can cause rare complications, such as:

- muscle spasms or weakness
- seizures
- kidney failure
- heart rhythm abnormalities
- shock
- brain swelling (cerebral oedema)

What can I do to prevent CHS?
Only stopping marijuana use completely will prevent CHS. Cutting down your use will not get rid of CHS. You may not want to believe that marijuana may be the underlying cause of your symptoms. This might be because you have used it for many years without having any problems, but CHS can take several years to develop. Quitting marijuana may lead to other health benefits, including:

- better lung function
- improved memory and thinking skills
- better sleep
- reduced risk of depression and anxiety

Where to get help for drugs
Below are some of the services available to help you quit marijuana and other drugs:

FRANK
Telephone: 0300 123 6600
Website: www.talktofrank.com

DEPARTMENTS SHOULD INSERT DETAILS FOR LOCAL DRUG SERVICES HERE.
Details should include:

- Service name
- Any limitations on population (e.g. age, gender, substances used)
- Contact details
- Whether patients can self-refer or require provider referral

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