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PRACTICE

EASILY MISSED?

Cannabinoid hyperemesis syndrome

Yaniv Chocron *chief resident*[1], Jean-Philippe Zuber *consultant*[2], Julien Vaucher *consultant and senior clinical lecturer*[1]

[1]Internal medicine, Lausanne University Hospital, Lausanne, Switzerland; [2]Internal medicine, St-Loup Hospital, Pompaples, Switzerland

What you need to know

- Cannabinoid hyperemesis syndrome is a new diagnosis, accounting for up to 6% of patients presenting to emergency departments with recurrent vomiting in one retrospective study
- People experiencing cannabinoid hyperemesis syndrome compulsively take hot showers or baths to alleviate symptoms
- The only known long term therapy for cannabinoid hyperemesis syndrome is cannabis cessation

A 26 year old man attends the emergency department with a four week history of diffuse abdominal pain and nausea, along with vomiting every 30 minutes. Laboratory test results show a sodium level of 124 mmol/L (reference range 135-145) and a creatinine level of 348 µmol/L (62-106). During the last six years he has sought medical care several times for similar episodes, but no precise diagnosis was made, despite multiple investigations (including abdominal ultrasound and computed tomography scan and upper and lower endoscopies). He admits smoking cannabis about 4-6 times a day for 13 years. His symptoms are only alleviated by taking hot showers and baths, which he takes 10 to 15 times a day. After rehydration and normalisation of renal function, he is discharged home with a psychiatric follow-up to support cannabis abstinence. Three years after cessation of cannabis consumption, he does not report any symptoms.

What is cannabinoid hyperemesis syndrome?

Cannabinoid hyperemesis syndrome (CHS) was first described in 2004[1] and associates cyclic nausea and vomiting with abdominal pain in regular cannabis users (defined, in the most comprehensive systematic review on CHS, as at least weekly cannabis use[2]). Typically, patients report compulsive hot showering or bathing to alleviate symptoms (encountered in 90-100% of reported cases and it has been proposed as a diagnostic criteria).[1-3]

Different mechanisms have been proposed to explain how, in certain individuals, the established anti-emetic properties of cannabis are overridden and CHS develops.[2 4] Approximately 100 cannabinoids have been identified,[5] and each potentially contributes differentially to disease mechanisms.[4] One hypothesis suggests that stimulation of enteric cannabinoid receptors 1 (CB1) inhibits gastric and intestinal motility,[6] possibly inducing vomiting related to CHS.[7] However, in a case series,[3] only 30% of patients suffering from CHS had delayed gastric emptying on scintigraphy.

Another hypothesis resides in stimulation of vascular CB1 receptors inducing splanchnic vasodilation.[8] As encountered in late stage cirrhosis, mesenteric congestion could thus contribute to the symptoms.[8] Exposure to hot water redistributes blood flow to the skin and could then explain symptom relief.[8] Based on observational and animal studies, it is also suggested that cannabis disrupts the hypothalamic-pituitary-adrenal axis, affecting homoeostasis of digestion and thermoregulation,[4] similar to cyclic vomiting syndrome.[3] Finally, it has been hypothesised that genetic variations in hepatic drug transforming enzymes, resulting in excessive levels of pro-emetic cannabis metabolites, may explain the differences in clinical presentations among cannabis users.[2] The type of cannabis is often not specified in publications. However, one observational study, including 2567 patients who presented to an academic emergency department with cannabis related conditions, suggested that CHS was more common in people exposed to inhalable cannabis.[9]

How common is it?

Evidence from a US retrospective study including 1571 patients showed that CHS affects up to 6% of patients consulting for recurrent vomiting in emergency departments.[3] Moreover, among regular cannabis smokers, about one third of them reports hot showers or baths as a means to relieve nausea and/or vomiting.[10] Extrapolating those results to the population of the United States, it is estimated that 2.1-3.3 million people might suffer from CHS annually.[10] In Colorado, which legalised cannabis in 2009, visits to emergency departments for cyclic vomiting doubled after legalisation.[11] An estimated 182 million

Correspondence to Y Chocron yaniv.chocron@chuv.ch

people worldwide were cannabis consumers in 2013, increasing to 192 million in 2016,[12 13] therefore CHS may represent an important diagnosis to consider in any patient consulting for recurrent vomiting.

Why is it missed?

In most cases, diagnosis is delayed.[2 14-16] In a small case series including eight patients,[14] the average number of emergency department visits before diagnosis was 7.1. In a systematic review based on individual data of 211 patients, the mean delay between symptom onset and diagnosis was 4.1 years.[2] Literature on CHS is limited, preventing its recognition by many physicians.[15-17] For instance, in a retrospective study examining charts of 494 patients visiting two emergency departments for vomiting or cyclic vomiting, a record of cannabis use was mentioned in only 19.4% of the cases, and the feature of symptoms alleviation by exposure to hot water was never documented.[16] Finally, cannabis is well known for its anti-emetic properties[18] (eg, in patients treated with chemotherapy), and any emesis related to its use may appear counterintuitive, further reducing identification of CHS.

Why does it matter?

Delayed diagnosis prolongs suffering and is the cause of multiple hospital admissions and unnecessary expensive investigations, such as radiating imaging, endoscopies, and even exploratory laparoscopies.[2 15 16 19] CHS may portend serious complications such as acute renal failure,[20] electrolyte disturbance, skin scalds,[1 21] or intestinal pseudo-obstruction.[22] Fatalities caused by CHS, probably associated with electrolyte disturbance and dehydration, have also been reported.[23] Besides health related conditions, CHS and consequent hot water use has been associated with high water bills and wastage.[24]

How is it diagnosed?

The diagnosis relies on history. A systematic review by Sorensen et al.[2] identified the main characteristics of patients with CHS (box 1). Most were regular users of cannabis presenting with severe cyclic nausea and vomiting.

Box 1: Main characteristics of patients with cannabinoid hyperemesis syndrome(adapted from Sorensen et al[2])

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

Percentages express the frequency of the characteristics found in the systematic review by Sorensen et al (maximal n=227)[2]

Urine drug screening may be useful in patients with unexplained recurrent vomiting, especially if they report no cannabis use. No other paraclinical investigation is necessary to establish the diagnosis of CHS, but electrolytes and renal function analyses are required to assess any complication, especially in cases of severe vomiting. Any abnormality in the clinical examination or in blood tests (eg, in tests of hepatobiliary function) should prompt further investigation. Cyclic vomiting syndrome should be considered in people who do not use cannabis or in patients who experience no relief after cannabis cessation, especially if vomiting onset is acute and duration of symptoms is less than one week.[25]

How is it managed?

The only long term effective therapy is cannabis cessation, with complete and permanent resolution of symptoms within the first two weeks after cannabis weaning. Long term cessation may require a psychiatric follow-up and/or pharmacological interventions.[15 26] In the acute phase, no evidence based management exists and care is essentially supportive with intravenous rehydration, especially in cases of acute renal failure and hyponatraemia. According to recent case series,[27 28] application of topical capsaicin on the abdomen may relieve symptoms in the acute phase. Capsaicin produces a heat sensation on the skin through activation of TRVP-1 receptors, which are known to interact with the endocannabinoid system, potentially explaining symptom relief.[28] Use of capsaicin cream is safe, inexpensive, and well tolerated.[29] Benzodiazepines have been proposed as a first line treatment in acute situations, based on their anti-emetic and, especially, anxiolytic effects.[29 30] Haloperidol and other antipsychotic drugs have also been successfully used in case reports.[31 32] These pharmacological approaches may be helpful in the acute phase to alleviate the gastrointestinal symptoms and pain, but they are not meant to become long term treatments as they themselves portend serious side effects and some may be addictive. Finally, most authors recommend avoiding opioids for pain relief, which can worsen the nausea.[2 29]

Education into Practice

- Do you know how many of your patients are regular users of cannabis?
- How many times have you had a patient with unexplained abdominal pain and vomiting? Did you ask them if hot water relieved their symptoms?
- What would you do differently before prescribing radiating imaging and/or endoscopies in patients with unexplained abdominal pain and vomiting?

How patients were involved in the creation of this article

The vignette in this article is fictitious. There was no direct patient involvement in the creation of this article.

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