Cannabinoid Hyperemesis Syndrome: Literature Review and Proposed Diagnosis and Treatment Algorithm

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Abstract: Cannabinoid hyperemesis syndrome (CHS) is characterized by cyclic vomiting and compulsive bathing behaviors in chronic cannabis users. Patients are typically diagnosed with CHS only after multiple and extensive medical evaluations, consequently without a clear etiology of their symptoms or treatment plan leading to symptomatic improvement. Increased healthcare provider awareness of CHS as a cause of nausea, vomiting, and abdominal pain coupled with an attentiveness to focused history taking—especially noting symptomatic improvement with prolonged exposure to hot showers or baths—can lead to effective treatment through cannabis cessation. We propose a diagnosis and treatment algorithm for physicians to follow when evaluating patients presenting with nausea, vomiting, and abdominal pain who are suspected to suffer from CHS.

Key Words: cannabinoid hyperemesis, cannabis, compulsive bathing, cyclic vomiting

Cannabinoid hyperemesis syndrome (CHS) is characterized by cyclic vomiting and compulsive bathing behavior in people who chronically use cannabis on a daily basis. The syndrome was first reported in 2004 in 9 patients in Australia.1 Subsequently, 22 cases in Canada, Great Britain, Spain, the Netherlands, New Zealand, and the United States have been reported.2-14 All patients were diagnosed with CHS after they had suffered for years with symptoms and had presented multiple times to healthcare facilities, receiving a variety of diagnostic tests. While the antiemetic effects of cannabis are widely known,15-17 the paradoxical emetic effect from chronic cannabis use is under-recognized by both healthcare providers and the public. Government- and nongovernment-sponsored websites often list the benefits and harms of cannabis use but fail to mention potential side effects of nausea, vomiting, or abdominal pain associated with chronic cannabis use.18-22 With newfound awareness in 2010 of CHS as possible cause for one of our patient's nausea, vomiting, and compulsive bathing behavior, we have since identified an additional 5 patients who we believe suffer from CHS. Likely, a number of chronic cannabis users with similar symptoms are utilizing a significant amount of healthcare resources for evaluation and treatment, yet continue to use cannabis without symptom resolution.

In this article we discuss the epidemiology of cannabis use and the number of people who are potentially at risk for CHS; offer a review of previously published CHS cases; describe the pathophysiology of cannabis both as an antiemetic and as a cause of cyclic vomiting; suggest how the pathophysiology of compulsive bathing behavior may improve the symptoms of CHS; and propose a diagnosis and treatment algorithm for patients suspected of suffering from CHS. We also examine areas of uncertainty and opportunities for potential research.

Epidemiology

Cannabis is the most widely used illicit drug in the United States among all age groups.23 In 2008, 2.2 million adolescents aged 12 to 17 used marijuana for the first time, more than any other illicit drug.24 While 42.6% of high school seniors...
reported using cannabis at least once in their lifetime, 5.4% use cannabis on a daily basis.\textsuperscript{18} CHS has been almost exclusively reported in people who began using cannabis daily in their teenage years.\textsuperscript{2–14} Therefore, chronic daily users of cannabis may be at the highest risk for developing CHS. There are presently 17.2 million students in the United States enrolled in grades 9 through 12.\textsuperscript{25} If approximately 20% (3.4 million) are enrolled in grade 12, then roughly 183,600 of current high school seniors are potentially at risk of developing CHS within the next few years if they continue to use cannabis daily. The risk of developing CHS depends on multiple known and unknown factors, including but not limited to how much cannabis is used on a daily basis and the method of use, as well as other confounding medical, psychiatric, ethnic, and socioeconomic conditions. Fourteen US states and the District of Columbia have legalized the use of medicinal cannabis,\textsuperscript{19} and other countries have decriminalized the possession or use of cannabis. Increased availability and use by patients who become chronic cannabis users as adults could result in a rise in the number of people who develop CHS.

The relatively few number of published cases about CHS could suggest that the diagnosis is uncommon; however, we propose that because CHS was first described only 7 years ago and the diagnostic symptoms are largely unknown

\begin{table}
\centering
\caption{Published cases of cannabinoid hyperemesis syndrome}
\begin{tabular}{lllllll}
\hline
\textbf{Author} & \textbf{Case} & \textbf{Age, y} & \textbf{Sex} & \textbf{Compulsive bathing} & \textbf{Age\textsuperscript{a}} & \textbf{Before vomiting\textsuperscript{b}} & \textbf{Before diagnosis\textsuperscript{c}} & \textbf{Symptom\textsuperscript{d}} \\
\hline
Allen et al\textsuperscript{1} & 1 & 23 & M & Yes & 19 & 3 & 1.3 & Improved \\
& 2 & 29 & F & Yes & 17 & 3 & 9 & Improved \\
& 3 & 44 & M & Yes & 16 & 6 & 12 & Improved \\
& 4 & 37 & M & Yes & 17 & 17 & 3 & Improved \\
& 5 & 21 & M & Yes & 12 & 5 & 4 & No cessation \\
& 6 & 38 & M & Yes & 17 & 17 & 4 & Improved \\
& 7 & 36 & F & Yes & 12 & 2 & 3 & Improved \\
& 8 & 21 & M & Yes & 14 & 3 & 0.5 & Improved \\
& 9 & 49 & M & No & 18 & 14 & 6 & No cessation \\
Boeckxstaens\textsuperscript{2} & 10 & 30 & M & Yes & 14 & — & — & — \\
Roche and Foster\textsuperscript{3} & 11 & 38 & M & Yes & — & — & 2 & Improved \\
Alfonso Moreno et al\textsuperscript{4} & 12 & 49 & F & Yes & 18 & 2 & 29 & Improved \\
Wallace et al\textsuperscript{5} & 13 & 30 & M & — & 18 & 7 & 5 & Improved \\
Chapyala and Olden\textsuperscript{6} & 14 & 38 & M & Yes & 18 & 17 & 3 & Improved \\
Singh and Coyle\textsuperscript{7} & 15 & 46 & M & Yes & — & — & — & Improved \\
Chang and Windish\textsuperscript{8} & 16 & 25 & F & Yes & 19 & 5 & 1 & Improved \\
Ochoa-Mangado et al\textsuperscript{9} & 17 & 25 & M & Yes & 19 & 1 & 7 & Improved \\
Sannarangappa and Tan\textsuperscript{10} & 18 & 34 & M & Yes & 19 & 5 & 10 & Improved \\
Sontinent et al\textsuperscript{11} & 19 & 22 & M & Yes & 16 & 5 & 0.2 & Improved \\
Watts\textsuperscript{12} & 20 & 32 & M & Yes & 16 & 13 & 3 & Improved \\
Donnino et al\textsuperscript{13} & 21 & 22 & M & Yes & — & — & 2.1 & Improved \\
& 22 & 23 & M & Yes & 20 & 1 & 1.7 & Improved \\
& 23 & 51 & M & Yes & — & — & 2 & Improved \\
Soriano-Co et al\textsuperscript{14} & 24 & 34 & M & Yes & 20 & 19 & 1 & Improved \\
& 25 & 34 & F & Yes & 13 & 19 & 2 & No cessation \\
& 26 & 26 & M & Yes & 14 & 9 & 5 & Improved \\
& 27 & 34 & M & Yes & 10 & 21 & 3 & Improved \\
& 28 & 38 & F & Yes & 15 & 15 & 8 & Improved \\
& 29 & 27 & M & Yes & 9 & 19 & 0 & No cessation \\
& 30 & 35 & M & Yes & 15 & 20 & 0 & No cessation \\
& 31 & 31 & F & Yes & 13 & 16 & 2 & Not improved \\
\hline
\textbf{Mean (SD)} & 32 (9) & 15.9 (3.0) & 10.2 (7.1) & 4.5 (5.6) \\
\hline
\textsuperscript{a}Age at onset of regular cannabis use in years. \\
\textsuperscript{b}Duration of daily cannabis use before cyclical vomiting in years. \\
\textsuperscript{c}Duration of illness before CHS diagnosis in years. \\
\textsuperscript{d}Symptom result. \\
M, male; F, female. \\
\end{tabular}
\end{table}
throughout the medical profession and among cannabis users, a significant number of cases might be unrecognized. Patients with CHS have often been diagnosed only after undergoing extensive and repeated testing for their symptoms over a period of several years with no previously identified, clear etiology. An extensive review of the literature was required for us to recognize that chronic cannabis use could be the cause of their patients’ paradoxical nausea and vomiting.

**Summary of Case Reports**

Thirty-one previously published cases of CHS are described in Table 1. Seventy-seven percent of patients reported were men. Most patients began chronic, daily cannabis use as teenagers (mean 15.9 years; SD 3.0; range 9–20), and symptoms of CHS developed after years of chronic daily use (mean 10.2 years; SD 7.1, range 1–21). Diagnosis of CHS did not occur until several years after the initial onset of symptoms (mean 4.5 years, SD 5.6; range 0–29). Use of cannabis multiple times daily was specified in all reports except for three cases where amount used was not specified. Amounts were described in terms of “cones,” “joints,” “bongs,” or “bags” per day or by frequency of inhalation in hours. Prior to diagnosis, all patients presented multiple times to healthcare facilities with similar symptoms and received multiple diagnostic imaging and invasive procedures without a clear diagnosis and treatment plan resulting in symptomatic improvement. Reported tests included abdominal x-ray, abdominal computerized tomography (CT), abdominal ultrasound, esophagastroduodenoscopy (EGD), colonoscopy, head CT, gastric emptying studies, upper GI with barium with or without small bowel follow through, capsule endoscopy, hepatobiliary iminodiacetic acid (HIDA) scan, and magnetic resonance cholangiopancreatography (MRCP). One patient received a neurology consultation and 2 patients received psychiatric consultations.

Previous reports described improvement in cyclic vomiting within 12 to 48 hours of hospital admission and administration of intravenous fluids. A recent case series of eight patients reported a significant decline in daily vomiting one week, on average, after cannabis cessation. Antiemetics, including metoclopramide, ondansetron, prochlorperazine, and promethazine, have not been effective in relieving nausea and vomiting at presentation. Significant symptom resolution following cannabis cessation was reported in cases where follow-up information was reported. Given the small number of cases reported and lack of clinical trials, it remains unclear whether intravenous hydration or cannabis cessation alone leads to symptom resolution and which, if any, antiemetics effectively improve symptoms.

**Cyclic Vomiting**

The pathophysiology of cannabis as a cause of cyclic vomiting is not completely understood. Several theories have emerged based on current understanding of the endogenous cannabinoid system. Delta-9-tetrahydrocannabinol (THC) is the principle active cannabinoid in marijuana; it binds to cannabinoid type 1 (CB1) and type 2 (CB2) receptors in human tissues. CB2 receptors are located mostly in immune tissue and thus may not have a role in emesis due to cannabis use. CB1 receptors are located in the central nervous system and enteric plexus. It is likely they mediate the anti-emetic effects of cannabinoids. However, chronic stimulation of these receptors may produce a paradoxical emetic response in susceptible individuals. THC has been shown to slow gastrointestinal motility in a dose-dependent manner and could induce symptoms via this neuromodulatory effect. One study demonstrated that nausea and vomiting can be provoked with a large intravenous dose of crude marijuana extract.

Diagnoses to consider when evaluating patients with cyclic vomiting include CHS, migraine headaches, hyperemesis gravidarum, Addison’s disease, psychogenic vomiting, bulimia, and cyclic vomiting syndrome (CVS). Unique characteristics of these diagnoses are listed in Table 2. The causes of CVS and psychogenic vomiting remain unclear and are the most confounding differentials when establishing a diagnosis of CHS. Unique to CVS is a family history of migraine headaches and psychological stressors, which are not associated with CHS. However, compulsive bathing behaviors and

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**Table 2. Differential diagnosis of cyclic vomiting**

<table>
<thead>
<tr>
<th>Diagnoses to consider with cyclic vomiting</th>
<th>Associated disease components and symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cannabinoid hyperemesis syndrome</td>
<td>Chronic cannabis use, compulsive bathing behaviors</td>
</tr>
<tr>
<td>Cyclic vomiting syndrome</td>
<td>Family history of migraines, psychological stressors</td>
</tr>
<tr>
<td>Hyperemesis gravidarum</td>
<td>Pregnancy</td>
</tr>
<tr>
<td>Psychogenic vomiting</td>
<td>Typically associated with conversion disorder or major depression</td>
</tr>
<tr>
<td>Bulimia</td>
<td>Binging/purging behavior to prevent weight gain</td>
</tr>
<tr>
<td>Addison disease</td>
<td>Fatigue, weight loss, hyperpigmentation, hypotension, hyponatremia, hyperkalemia</td>
</tr>
<tr>
<td>Migraine headaches</td>
<td>Unilateral headache with/without aura, photophobia</td>
</tr>
</tbody>
</table>
chronic cannabis use are distinctive to CHS, unlike other diagnoses associated with cyclic vomiting.

**Compulsive Bathing**

Compulsive bathing behaviors were described in all but 2 reported cases. Though not clearly defined, compulsive bathing is suggested when patients take multiple hot showers or baths daily or take a single bath or shower lasting several hours. Patients diagnosed with CHS report temporary relief of nausea and vomiting with prolonged and repeated exposure to hot water through baths or showers. Bathing duration was reported in one case series to last from 3 to 6 hours at a time with a mean of 5 hours daily. One patient spent “all day” in the bathtub “300 out of 365” days during the past year, ran out of hot water at home, and used a shower in an adjacent hospital room when the hot water in his room ran out. Another patient reported taking “20 lengthy showers each day” and applying hot water bottles to his abdomen to help relieve symptoms.

Compulsive hot water bathing is thought to relieve nausea and cyclic vomiting through either brain response to core body temperature changes resulting from hypothermic effects of THC or activation of CB1 receptors in the hypothalamus, which regulates body temperature. Cannabinoids may also exert an anxiolytic effect by reducing the psychological stress from persistent nausea and vomiting. Regardless of the mechanism, other clinical conditions have not been identified in the literature where consistent relief of nausea and vomiting is achieved with hot water exposure. Since compulsive bathing and symptom relief were clearly described in nearly all CHS patients, the relief of cyclic vomiting with hot water exposure in chronic cannabis users should be considered a pathognomonic feature of CHS.

**Diagnosis and Treatment**

Increased healthcare provider awareness of CHS and focused history taking—especially noting symptomatic improvement with prolonged exposure to hot showers or baths in chronic cannabis users presenting with cyclical vomiting—can lead to effective treatment through cannabis cessation. Clinical characteristics for the diagnosis of CHS have been proposed. However, we encourage clinicians to use the diagnosis and treatment algorithm shown in Figure 1 for patients with suspected CHS to help reduce unnecessary testing and utilization of healthcare resources. Initially, physical examination and history taking is recommended for patients presenting with nausea, vomiting, and abdominal pain to rule out life-threatening causes or diagnoses that confer significant potential morbidity to the patient. Prompt and appropriate diagnostic testing and treatment should be pursued for patients with suspected conditions noted in Figure 1.

If life-threatening diagnoses are not suspected, we suggest the healthcare provider ask the patient if symptoms of nausea, vomiting, and abdominal pain improve after taking a hot shower or bath. Such inquiry prior to questions about cannabis use is warranted, as patients may be reluctant to offer an accurate drug use history or may deny that cannabis use is contributing to their symptoms. If patients report relief from their symptoms with hot water exposure, it is important to determine the extent to which bathing activity is compulsive by asking how long and how often they take a hot shower or bath. Patients with CHS often take hot baths or showers lasting up to several hours and/or multiple times each day. If compulsive bathing behavior in hot water is confirmed, the clinician should ask the patient about their use of cannabis products. Since discussing substance use can be a sensitive topic for patients, healthcare providers are advised to describe a possible relationship between cannabis use and the patient’s symptoms before inquiring about cannabis use. Informed patients may be more likely to accurately detail their cannabis use if they understand that cannabis may be the cause of

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**Fig. 1 Diagnosis and treatment algorithm for cannabinoid hyperemesis syndrome.** Diagnoses to consider when a patient presents with nausea include, but are not limited to acute hepatitis, adrenal insufficiency, bowel perforation, bowel obstruction, cholangitis, cholecystitis, diverticulitis, ectopic pregnancy, gastroparesis, myocardial infarction, nephrolithiasis, pancreatitis, pelvic inflammatory disease, pregnancy, and ruptured or dissecting aortic aneurysm.
symptoms that lead them to seek medical assistance and that cessation of cannabis may lead to symptom improvement. Clinicians should elicit details as to when cannabis use first began, how often and how much it is used, and when symptoms of nausea, vomiting, and abdominal pain were first experienced. If symptoms began at least 1 year after chronic daily cannabis use began, a diagnosis of CHS is likely. Furthermore, if symptoms previously improved during cannabis cessation and reoccurred after resuming cannabis use, the diagnosis is further supported. It is advised that clinicians initially avoid unnecessary laboratory testing and imaging unless otherwise clinically indicated. If a patient denies cannabis use yet states that bathing in hot water relieves nausea and vomiting symptoms, a urine drug screen for THC is suggested. Patients testing positive should be informed of the test results, and then re-questioned.

Once a presumptive diagnosis of CHS has been made, patients should be evaluated for signs and symptoms of volume depletion. If so evident, a patient may require intravenous hydration in a clinic, an emergency department, or hospital, depending on symptom severity. Continuous observation and treatment should not be necessary for more than 48 hours given that symptoms improve and cannabis use has ceased. Be aware that cyclic vomiting may be refractory to antiemetics.

Intravenous hydration may not be required provided that the presumptive CHS diagnosis is accepted, the patient is compliant with cannabis cessation, symptoms are mild, and oral liquids can be tolerated. If symptoms resolve, additional counseling and resources to assist with continued cessation of cannabis use should be provided. Clinicians might consider a urine drug screen after symptom resolution to confirm the absence of THC, which would further support a CHS diagnosis. However, clinical management would not change if the patient’s symptoms have resolved with reported cannabis cessation. Thus, a repeat urine drug screen might not be clinically useful.

If symptoms do not improve, healthcare providers are encouraged to ask the patient about continued cannabis use and secondhand exposure to cannabis. If confirmed, the provider should offer additional information resources and encourage the patient to cease cannabis use or secondhand exposure. If the patient denies use, a re-evaluation and urine drug screen is warranted to identify other possible causes for their symptoms.

Summary

CHS is characterized by chronic cannabis use, cyclic vomiting, and compulsive bathing behavior. As a potentially under-recognized cause of nausea, vomiting, and abdominal pain, the effects of CHS on undiagnosed patients can lead to decreased quality of life and productivity and result in repeated and unnecessary overuse of healthcare resources. Patients have typically been diagnosed with CHS only after receiving multiple and extensive medical evaluations over the course of months to years without a clear diagnosis. Earlier recognition and subsequent cannabis cessation can lead to symptom resolution and fewer trips to emergency departments or physician offices where additional testing and expense is likely to occur.

We suggest that focused history taking and physical examination with minimal testing can assist in eliminating other causes of nausea and vomiting while identifying CHS as a possible diagnosis. Primary care, emergency room, hospital physicians, and other healthcare providers are encouraged to ask patients presenting with nausea, vomiting, and abdominal pain if symptoms improve after taking hot showers or baths, and if so, to then inquire about cannabis use—the amount used and length of use. For patients who have used cannabis on a daily basis for more than one year, whose history suggests improvement of cyclic vomiting with compulsive hot water bathing; and who show no signs or symptoms of dehydration requiring intravenous fluids, we recommend cannabis cessation and primary care follow-up. Providers should be aware that patients might deny cannabis use as cause of their symptoms and, therefore, are at risk of continuing cannabis use. Some patients may doubt the presumed diagnosis and fail to follow up or might seek other medical opinions. This could result in repeated testing in other healthcare settings without identification of a clear diagnosis or provision of a treatment plan to alleviate symptoms. A lack of available information detailing side effects from chronic cannabis use warrants that government and non-government Internet sites related to cannabis use enumerate and update the published side effects of cannabis to include cyclic vomiting associated with chronic use. We also suggest that cannabis dispensaries provide CHS information to their customers, advising them to discuss an appropriate diagnosis and treatment plan with their physician.

Future studies are needed to better estimate the prevalence of CHS. Given the projected increased use of legalized medicinal cannabis in the United States, we suggest the number of CHS cases could increase, especially in states where patients have more consistent access to cannabis that can be used on a daily basis. Additionally, studies are needed to determine the risk factors for developing CHS, e.g., underlying medical, psychiatric, ethnic, or socioeconomic conditions as well as specific species, amount, potency, and method of inhalation of cannabis.

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