Case Series and a Review of Cannabinoid Hyperemesis Syndrome

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Abstract

Cannabionoid hyperemesis syndrome (CHS) is a condition observed in patients with chronic use of cannabis. It is characterized with GI symptoms including nausea, vomiting, abdominal pain and diarrhea. The patients tend to be chronic abusers for several years and experience these symptoms in a cyclical manner similar to the cyclical vomiting syndrome. They find relief after taking hot baths, a pathognomonic feature of CHS. We hereby describe 3 cases who presented with clinical features consistent with CHS. Cannabis acts through CB1 and CB2 receptors located in brain and gastrointestinal tract, respectively. There are no standard therapeutic measures available for management of CHS. We propose the idea of using short-acting cannabinoids including dronabinol. Also review of literature suggests treatments with drugs including clonidine, lorazepam and risperidone. Recent endeavors on legalization of recreational cannabis use have initiated several debates and we should be mindful of CHS as one of its long-term complications.

Introduction

Cannabis is a widely used drug of abuse in the United States (US) with over 16.7 million users reported in 2009 [1]. Known for its psychedelic effects, it is mostly commonly abused by young individuals. Cannabis is also utilized by the medical field for a number of medicinal purposes, some of which have been well known for centuries. Most recently, the role of Cannabis as a medicinal agent has led to debates within several states about its legalization for non-medicinal or recreational use [2]. As of January 2014, Colorado became the first state to legalize cannabis for recreational use. Chronic cannabis users who are exposed to its active chemical ingredient, Δ9 Tetrahydrocannabinol (THC), develop addiction at an early age. Many quit its use, but those who continue its use can sometimes develop certain unusual illnesses. One such condition known to us is the “Cannabinoid Hyperemesis Syndrome” (CHS), first described in 2004 by Allen and colleagues [3].

CHS is associated with a history of first or second hand exposure to cannabis for more than a decade, and it is almost exclusively reported in people who began daily use of cannabis during their teenage years [2, 4]. The affected individuals develop episodic nausea, vomiting, abdominal pain and sometimes diarrhea. These vomiting episodes are cyclical, occurring every few weeks to months and lasting for days to weeks [1]. The acute episode develops spontaneously; some have been reported to be associated with exposure to foods that affected individuals dislike or after the ingestion of heavy meals. These patients almost exclusively find symptomatic relief after taking a hot water bath [2]. During these episodes they spend hours taking a warm shower or a hot water bath. We present three such cases of CHS who presented during exacerbation of their symptoms.

Case Descriptions

Case 1

A 45 year-old Caucasian man presented with a 10 day history of nausea, vomiting, generalized colicky abdominal pain and diarrhea. He found some relief of his symptoms with the use of narcotics but noticed significant relief after a hot bath. The patient was agitated and upset when he had no access to a hot shower in the emergency room but was equally content after he took a warm shower. He had similar presentations to several emergency rooms in the last 8 years and was hospitalized on multiple occasions. Some of these episodes were associated with development of acute renal failure secondary to dehydoration, followed by renal recovery after intravenous (IV) fluid hydration. Esophagogastroduodenoscopy (EGD) in the past had shown reflux esophagitis and gastritis, likely from constant retching. He was also diagnosed with gastroparesis and gastroesophageal reflux disease and was on a proton pump inhibitor. He had been smoking cannabis from the age of 9 years and continued to abuse the drug.

On physical examination there was no abdominal tenderness but bowel sounds were hyperactive. His oral mucous membranes were dry, suggesting dehydration. He had scalded skin on his back and behind his neck as a result of taking showers for several hours. He was obese with a body mass index...
Previous hypertension and obesity. The mechanism, although not fully understood, could be related to modulating inflammatory and stress responses. THC works by stimulating the G protein-coupled CB receptors, two subtypes of which are known, namely the CB1 and CB2 receptors [5]. CB1 receptors are expressed in the CNS. CB2 receptors are expressed in gastrointestinal immune cells as well as the myenteric and Meissner’s plexus of the small bowel. CB2 receptors are likely associated with down-regulation of intestinal inflammation, visceral pain, and motility [7]. A naturally occurring form of THC-like peptide, which has been termed as ‘anandamide’, is produced in our body. The name of this protein was derived from the Sanskrit word “Anand”, which means bliss or pleasure, a commonly experienced feeling described by Cannabinoid abusers. Anandamide is a neuromodulator which activates THC receptors in the brain to produce effects similar to those seen after endorphins and enkephalins act on opioid receptors [5].

Individuals who abuse cannabis for several years tend to develop obesity. The mechanism, although not fully understood, could involve cannabinoid receptors in the brain which regulate feeding behavior and energy expenditure. THC can bind to CB1 receptors located in the hypothalamus, resulting in decreased satiety and increased food intake. This effect is thought to contribute to the development of obesity in cannabis abusers.

**Case 3**

A 31-year-old man presented with a 4-day history of episodic sharp epigastric abdominal pain and vomiting. The symptoms usually lasted for 8 hours and were relieved after taking hot baths. He was an active cannabis abuser and had been experiencing these episodes of abdominal pain with vomiting for the last 6 months. He had lost his appetite due to chronic nausea, which led to weight loss of 70 lbs over this period of time and had a BMI of 17.5 on current presentation.

Previously he was found to have H. Pylori antigen in his stool and had completed triple antibiotic therapy; however the vomiting and abdominal pain persisted. He also had an EGD, which only showed reflux esophagitis. On multiple previous hospitalizations his pancreatic lipase level was elevated and CT scans of his abdomen only showed some focal changes in the pancreas. His recurrent abdominal pain was labeled as chronic pancreatitis in the past and he was placed on pancreatic enzyme replacement therapy. There was still incomplete relief from his symptoms and subsequent endoscopic ultrasound did not show any abnormalities in the pancreas. On physical examination he had mild tenderness in his left upper quadrant but no rebound tenderness.

His laboratory data showed a positive urine drug screen with no abnormalities detected on his electrolyte panel. The amylase and lipase levels were normal during his admission with a normal appearing pancreas on abdominal CT scan. Based on his history of cannabis abuse with episodic abdominal pain, nausea and vomiting; along with history of symptomatic relief by taking hot baths, he was presumptively diagnosed with CHS. The previous episodes of pancreatitis were suspected to be secondary to transient pancreatic ischemia induced by chronic marijuana abuse via activation of CB1 receptors. Oral diet was stopped and his symptoms slowly improved over 5 days. Hot baths continued to give him symptomatic relief.

Before discharge he was able to tolerate an oral diet. The patient was advised to stop using cannabis and was offered rehabilitation. He was additionally prescribed marinol and clonidine to assist with withdrawal.

**Discussion**

Cannabis Sativum is a species of plant from which the active chemical ingredient Δ9-Tetrahydrocannabinol is obtained. THC acts on the central nervous system (CNS) causing psychedelic effects, which include visual hallucinations, a sense of calmness, increased hunger, stimulatory ideation and psychomotor retardation. It also acts on the gastrointestinal tract (GIT) causing diarrhea secondary to stimulation of colonic THC receptors. The stool tends to be loose and watery due to the drug’s effect in expediting intestinal transit time, and subsequently decreasing the amount of water absorbed in the colon [5]. In addition, there are reports of substances used in the preparation of cannabis, such as preservatives or pesticides, which may also contribute to the symptoms of CHS [6].

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be explained by the increased desire for food caused by THC’s stimulation of the hunger center in the hypothalamus. THC is a lipophilic substance which tends to be stored in the adipocytes. Selective breeding of Cannabis sativum has increased the plant’s average THC content from 0.75% to as high as 16% [8], which may lead to an even greater concentration of THC to be retained in adipocytes. Obese individuals tend to have sustained levels of THC in their system even several days after their last exposure, which can lead to recurring effects of the drug. This phenomenon could have been the effect seen in the patients described in cases 1 and 2, who were classified as obese and pre-obese according to their BMI, respectively.

The most commonly noted GIT symptoms associated with CHS are nausea, vomiting, diarrhea and abdominal pain. CHS can be considered as a sub-type of CVS, which includes a broad range of clinical symptoms grouped together under this syndromic illness. The peculiar characteristic in CHS is that affected patients tend to find relief from nausea and vomiting after a hot bath. This mechanism is likely due to peripheral vasodilatation following exposure to warm water. This can be explained by an increase in cutaneous blood flow after the exposure to warm water, which drives blood away from the mesenteric circulation thereby decreasing the effect of THC on the GIT. However, this habit is a learned behavior and it may not be practiced during initial presentations [9]. All three of the patients described developed this behavior for relief of their symptoms. Some individuals may try to smoke cannabis during their exacerbations without any relief [3, 10]. Usually patients are anxious during episodes of CHS with increased sweating, tachycardia and repetitive retching [9, 11]. In patients with high clinical suspicion for CHS based on history and physical exam, extensive medical testing is not necessary [2]. Endoscopy may reveal associated esophageal and gastric mucosal trauma from retching [9]. EGD performed in our patients described above showed gastritis and reflux esophagitis in case 1 and case 2 respectively. The diagnosis of CHS becomes more obvious when patients present with episodic abdominal pain with nausea and vomiting for months to years and only find symptomatic relief with hot baths [12].

There have been published case reports on CHS. We present a series of 3 cases diagnosed with CHS. Case 1 and case 2 were found to have renal failure with elevated creatinine that was secondary to hypovolemia as a result of dehydration from repeated vomiting and diarrhea with poor intake of fluids. Over several years, episodes of acute renal failure from repeated episodes of hyperemesis and diarrhea may lead to irreversible renal injury leading to chronic renal insufficiency. Therefore, chronic renal failure can be considered as a long-term complication of CHS. In case 3 we also noted recurrent pancreatitis, another possible complication of CHS. This was speculated to be the effect of CB1 receptor induced transient pancreatic ischemia causing episodic pancreatitis.

There are no published retrospective studies or prospective trials on management of CHS. Review of literature has shown that the majority of patients receive symptomatic treatment and achieve resolution of an acute exacerbation after a period of hours to days. It should be noted that vomiting associated with CHS is usually refractory to antiemetics [2]. Although the patients described above recovered in a similar fashion with symptomatic treatment, prevention of these episodes with drug therapy would be a reasonable approach of management of this condition. We propose the idea of prescribing medical forms of THC, such as dronabinol or marinol, which are short acting cannabinoid receptor agonists usually used for the treatment of chemotherapy-induced nausea and vomiting. They can be given on a daily basis with a slow taper over months and have shown some utility in cannabis dependence [13,14]. However, it is unknown whether a cannabinoid receptor agonist would perpetuate or relieve the symptoms of CHS. We also would like to propose the idea of using clonidine, a centrally acting α-adrenergic antagonist in patients suffering from CHS. The rationale comes from the idea of inhibiting the adrenergic stimulation that causes vomiting and diarrhea. Roelofs et al, suggested a large dose of risperidone has been found to show some benefit in treating these episodes of CHS [15]. Nicholson et al, published a review which proposes the use of lorazepam for treatment of acute symptoms [6]. Hickey et al, recently published a case report of a patient with CHS presenting with CHS and intractable vomiting [16]. The patient was treated with a parenteral dose of haloperidol with relief of symptoms with 1 hour. Haloperidol could be considered in acute states especially when patients are agitated. For treatment of cannabis dependence, the only therapy reported to be of benefit for chronic treatment is cessation of cannabis use and cognitive behavior therapy with motivational enhancement [9,17].

We are aware that cannabis is a common drug of abuse and CHS has been a fairly new illness that has been described in clinical literature. However, with ongoing discussions for the legalization of recreational cannabis use and its recent approval in certain states in US in addition to its current medicinal use, we may encounter an increase in the number of CHS cases in the United States [2]. With this in mind, additional studies would be beneficial to determine potential risk factors for developing CHS with elimination of confounders like nicotine use, which is common among this group of drug abusers [6]. There are no standardized approaches for its treatment but some potential interventions that could be considered are dronabinol, clonidine and lorazepam. Clinical trials and retrospective case/control or cohort studies need to be undertaken to help determine treatment approaches with drugs for individuals who suffer this incapacitating illness for several years.

Author contributions:

Yezaz A Ghouri: Acquisition of case series, review and interpretation of available literature, and drafting of manuscript.

Jay Chouhan: Acquisition of case series and help with review of available literature.

Lauren Hoffman: Acquisition of case series and help with review of available literature.

Sushovan Guha: Critical review of available literature, revision of manuscript for important intellectual content, administrative, technical, or material support and supervision.

References


