Capsaicin Cream for Treatment of Cannabinoid Hyperemesis Syndrome in Adolescents: A Case Series

Jessica Graham, MD,[a] Michael Barberio, PharmD,[b] George Sam Wang, MD[a]

abstract

Cannabinoid hyperemesis syndrome (CHS) is an underrecognized diagnosis among adolescents. In the adult literature, it is characterized as nausea, vomiting, and abdominal pain in patients with chronic marijuana use. CHS is often refractory to the standard treatment of nausea and vomiting. Unconventional antiemetics, such as haloperidol, have been successful in alleviating symptoms; however, even 1 dose of haloperidol can lead to grave adverse effects, such as dystonia, extrapyramidal reactions, and neuroleptic malignant syndrome. The use of topical capsaicin cream to treat CHS has been well described in the adult literature. This treatment is cost-effective and is associated with few serious side effects. Here, we describe 2 adolescent patients with nausea, vomiting, and abdominal pain in the setting of chronic cannabis use whose symptoms were not relieved by standard antiemetic therapies, but who responded well to topical capsaicin administration in our pediatric emergency department. We also discuss the pathophysiology behind capsaicin's efficacy. These are the first reported cases in which capsaicin was successfully used to treat CHS in pediatric patients.

Cannabinoid hyperemesis syndrome (CHS) is a clinical diagnosis that has been described in patients who use cannabis chronically.[1–5] It is characterized by significant nausea, abdominal pain, and cyclic vomiting, which are often relieved by hot bathing.[4–14] Most patients receive significant medical evaluation without significant findings and are refractory to standard medical therapies.[1,3–7] We present 2 adolescent patients with delayed diagnosis of CHS whose symptoms improved with application of capsaicin cream.

CASE PRESENTATIONS

Case 1

A previously healthy 16-year-old girl presented to an outside emergency department (ED) with 1 week of nausea, vomiting, and abdominal pain. She reported chronic intermittent epigastric pain that had significantly worsened over the previous week and was now associated with nausea and vomiting. She denied fever, diarrhea, dysuria, or hematuria. Her last menstrual period was 1 week before and she denied recent sexual activity. She denied ethanol use but did admit to cannabis use. Vital signs were a temperature of 36.8°C, blood pressure (BP) of 106/63 mm Hg, heart rate (HR) of 103 beats per minute, respiratory rate (RR) of 16 breaths per minute, and pulse oxygen saturation (Spo_2) of 99%. She complained of diffuse abdominal pain, but had a soft abdomen without peritoneal signs. Laboratory testing, including a basic metabolic panel, complete blood count,

[a]*Section of Emergency Medicine, Department of Pediatrics, University of Colorado Anschutz Medical Campus, and* [b]*Department of Pharmacy, Children's Hospital Colorado, Aurora, Colorado*

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Address correspondence to Jessica Graham, MD, Pediatric Emergency Medicine, University of Colorado at Denver–Anschutz Medical Campus, 13123 E 16th Ave, B251, Aurora, CO 80045. E-mail: jessica.kraynik@childrenscolorado.org

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lipase, liver function tests, urinalysis, and a urine pregnancy test were significant only for a potassium level of 3.2 mmol/L, bicarbonate of 28 mmol/L, and a urinalysis revealing 40 mg/dL ketones, trace blood, and 30 mg/dL protein. She received 4 mg intravenous ondansetron, 10 mg metoclopramide, a 1000-mL normal saline bolus, and 30 mL of an oral lidocaine/diphenhydramine/aluminum and magnesium hydroxide solution. She left against medical advice before undergoing a computed tomographic scan despite expressing that there was no improvement in her symptoms.

The next evening, the patient presented to our institution with continued abdominal pain, nausea, and emesis. A detailed history revealed chronic cannabis use, which increased over the last week in attempts to treat her nausea and abdominal pain (multiple times per day). She could not identify alleviating or worsening factors. Her vital signs were a temperature of 36.6°C, HR of 80 beats per minute, BP of 113/74 mm Hg, RR of 16 breaths per minute, and Spo_2 of 97%. Her pain was 6 out of 10 possible points. On examination, she exhibited voluntary guarding with tenderness in her left upper quadrant and epigastric region; her abdomen was soft and nondistended without peritoneal signs. She was given 4 mg sublingual ondansetron and 5 mg oral oxycodone without improvement in her nausea or abdominal pain. Due to a history of cannabis use, the refractory nature of abdominal pain, and an otherwise negative diagnostic workup, CHS became the working diagnosis. After the risks and benefits were discussed, she verbally agreed to try capsaicin cream for the treatment of CHS. Capsaicin cream, 0.025% (1-mm-thick coating), was applied to her abdomen. Thirty minutes after capsaicin was applied, her pain decreased to a 3 out of 10 possible points and her nausea resolved. The patient did report the side effect of a mild "burning sensation" on her abdomen where the cream had been applied but was overall satisfied by the symptom relief. She had improvement in abdominal tenderness on examination and was discharged from the hospital.

Case 2

A 20-year-old man with moderate persistent asthma was seen in our ED with abdominal pain and vomiting. He admitted to being acutely intoxicated with marijuana. His vital signs were a temperature of 36.8°C, BP of 139/85 mm Hg, HR of 139 beats per minute, RR of 16 breaths per minute, and Spo_2 of 95%. Examination was significant for epigastric tenderness, but he had a soft abdomen and no peritoneal signs. He was given 4 mg oral ondansetron and 15 mL of an oral aluminum/magnesium hydroxide/diphenhydramine/lidocaine/simethicone solution. He subsequently tolerated oral fluids and was sent home with ondansetron and ranitidine for presumed gastritis.

One week later, he returned complaining of persistent abdominal pain and vomiting. Since his initial visit, he had been taking ranitidine twice daily and ondansetron nearly daily, but suffered from worsening pain. He reported that his pain was migratory, traveling from his right lower to right upper to left upper quadrant to his epigastric region. He had 3 additional episodes of nonbloody emesis since his last visit. He endorsed at least twice-daily marijuana use for >1 year and that his abdominal pain improved with hot showers. He denied fever, diarrhea, dysuria, or hematuria. Vital signs were a temperature of 36.3°C, BP of 125/73 mm Hg, HR of 73 beats per minute, RR of 12 breaths per minute, and Spo_2 of 96%. Abdominal examination revealed a soft, nondistended abdomen without peritoneal signs. Laboratory testing, including a basic metabolic panel, complete blood count, liver function tests, and lipase, was significant only for bilirubin of 1.4 mg/dL. An ultrasound of the abdomen was normal. Negative workup, chronic cannabis use, and symptom improvement with hot showers led to a presumed diagnosis of CHS. The patient verbally agreed to try capsaicin cream for the treatment of CHS. Capsaicin cream, 0.025% (1-mm-thick coating), was applied to his abdomen. Thirty minutes after application, the patient reported marked improvement in abdominal pain and nausea. He also complained of a burning sensation over his abdomen but was satisfied with the symptom relief and was discharged.

DISCUSSION

CHS was first described in 2004 in a case series of 9 patients who used cannabis chronically and who exhibited cyclic vomiting and compulsive bathing with hot water.[1] There have been several case series and reports describing patients with chronic marijuana use and similar associated symptoms.[4,6,8–15] Although CHS has mainly been described in adult patients, health care providers should also be aware that this diagnosis can occur in adolescents.[7,16] In 1 published case, a 17-year-old presented to the ED 5 times for abdominal pain, nausea, and vomiting over the course of 1 year.[7] He received an extensive medical workup, which was negative. Consistent with CHS, his symptoms were relieved by hot showers and only completely resolved after the cessation of marijuana use.

The pathophysiology of CHS is not well understood at this time. In some circumstances, cannabis has antiemetic effects; therefore, the concept of it causing hyperemesis is counterintuitive.[3,17,18] Marijuana's effects on the nausea and vomiting

centers have been hypothesized to occur via CB1 and CB2 receptors in the preoptic dorsal ganglia, hypothalamus, hippocampus, cerebellum, and peripheral enteric nerves of the parasympathetic system.[3,17–19] These receptors are linked to the hypothalamic-pituitary-adrenal axis and are thought to mediate the release of prolactin, gonadotropin, and growth hormone (anterior pituitary hormones) and corticotropin. The proposed mechanism of cyclic vomiting syndrome, a gastrointestinal condition with symptoms comparable to CHS, is a disturbance of the hypothalamic-pituitary-adrenal axis.[13,20] It has been proposed that CHS may function by a similar mechanism, acting on cannabinoid (CB) receptors linked to the axis.

The interesting, almost pathognomonic, characteristic of CHS is the relief of symptoms by hot showering or bathing. This effect was initially proposed to be motivated by impaired thermoregulation mediated by the stimulation of CB receptors in the preoptic area.[13] However, the receptor that may actually deserve credit for this phenomenon in CHS is the transient receptor potential vanilloid-1 receptor (TRPV1), a nociceptor found in the peripheral nervous system that is involved in the pain relief we feel from endocannabinoid stimulation and which also regulates body heat.[21] TRPV1 is activated by exposure to scalding heat (109°F).[22–24] Interestingly, capsaicin also stimulates the TRPV1 receptor.[24] Lapoint[25] identified the clinical advantage of the physiologic link between cannabis, heat, and capsaicin when they applied the chili pepper derivative (0.075% capsaicin) to the abdomens of several adult patients with CHS and observed relief of their nausea, vomiting, and abdominal pain. Additional case reports subsequently also described the treatment of CHS with application of 0.075% capsaicin to the abdomen and 0.025% capsaicin to the back, arms, and abdomen.[26,27]

Currently, there are no laboratory or radiographic tests that are diagnostic for CHS. Studies are used to rule out common abdominal pain diagnoses. Both histories and symptoms were consistent with CHS, and capsaicin cream provided symptomatic relief where conventional antiemetics and medical treatment had failed. Other treatment modalities for CHS have included intravenous fluids, antiemetics, and haloperidol.[28] The only adverse effect our patients described was a "burning sensation" on their skin. Our patients did not return to our ED after treatment with capsaicin cream. By effectively alleviating symptoms in our patients, we prevented further unnecessary medical workup as well as unnecessary treatment with high-risk medications, including opioid analgesics. Our case report is limited by describing only 2 clinical cases involving patients seen in our pediatric ED. Thus, the effectiveness of capsaicin may not be universal for all patients with CHS. Although the preferred long-term treatment would be cessation of cannabis use, acute treatment with capsaicin is inexpensive, with few reported side effects.

Recent estimates indicate that 7.4% of all adolescents are current users of marjiuana.[29] In Colorado, where both retail and recreational marijuana is now legal, the number of patients presenting to the ED for cyclic vomiting nearly doubled after liberalization of medical marijuana.[30] As marijuana becomes more publicly available, health care providers, including pediatricians, need to be vigilant about potential health effects, including the symptoms of CHS. Although more research is needed on the potential benefits of capsaicin cream and the use for CHS, application of capsaicin cream should be considered as a cost-effective treatment and diagnostic option.

ABBREVIATIONS

BP: blood pressure
CB: cannabinoid
CHS: cannabinoid hyperemesis syndrome
ED: emergency department
HR: heart rate
RR: respiratory rate
Spo_2: pulse oxygen saturation
TRPV1: transient receptor potential vanilloid-1 receptor

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