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Abstract

Legalization of marijuana use will increase the number of people who will become long-term users. A prior medical record review study in Australia, in 2004, identified 19 chronic marijuana users who entered the emergency department with recurrent vomiting associated with abdominal pain. Routine treatment of the nausea and vomiting, associated with the chronic marijuana abuse, with antiemetics is ineffective in patients with cannabinoid hyperemesis syndrome. Narcotics do not relieve the abdominal pain but may cause worsening rebound pain. The best treatment of cannabinoid hyperemesis syndrome was found to be abstinence from the recreational use of marijuana. It is important for advanced practice nurses to place cannabinoid hyperemesis syndrome in their differentials of patients presenting to the emergency department with recurrent nausea, vomiting, and abdominal pain. They need to be knowledgeable about cannabinoid hyperemesis syndrome to provide the proper management of care for this specific medical condition.

Legalization of marijuana use will increase the number of people who will become long-term users. A prior medical record review study in Australia, in 2004, identified 19 chronic marijuana users who entered the emergency department with recurrent vomiting

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associated with abdominal pain. In the study, long-term users were identified as those persons using marijuana on a daily basis or monthly. The symptoms improved after taking hot showers or hot baths. The hot showers and baths likely worked to correct the disequilibrium of the thermoregulatory system of the hypothalamus affected by the chronic marijuana use (Allen, DeMoore, Heddle, & Twartz, 2004). Usually, the patients did not associate the use of marijuana for precipitating the symptoms of nausea, vomiting, and abdominal pain (Allen et al., 2004). With more recent research, these symptoms of recurrent nausea, vomiting, and abdominal pain have been identified as a medical condition named cannabinoid hyperemesis syndrome (CHS). The triad of symptoms of CHS is identified in recent studies as nausea, vomiting, and abdominal pain, relieved by taking hot baths or showers (Simonetto, Oxentenko, Herman, & Szostek, 2012; Sontineni, Chaudhary, Sontineni, & Lanspa, 2009; Soriano-Co, Batke, & Cappell, 2010; Sun & Zimmerman, 2013). These studies supported the findings of Allen et al.'s (2004) study. Literature further identifies three phases of cyclic vomiting: prodromal, hyperemetic, and the recovery phase (Galli, Sawaya, & Friedenberg, 2011). Routine treatment of the nausea and vomiting with antiemetics usually is ineffective in patients with CHS. Narcotics do not relieve the abdominal pain but may cause worsening rebound pain. The best treatment of CHS was found to be abstinence from the use of marijuana (Allen et al., 2004; Simonetto et al., 2012; Sun & Zimmerman, 2013).

It is important for advanced practice nurses to be able to identify CHS as a potential differential in patients presenting to the emergency department with recurrent nausea, vomiting, and abdominal pain. They need to be knowledgeable about CHS to provide the proper management of care for this specific medical condition.

Case Study

A 17-year-old adolescent boy entered the emergency department with recurrent nausea and vomiting complaining of epigastric abdominal pain. As he left triage in a wheelchair, provider noticed that he appeared pale, his head was down inside a bucket, he was diaphoretic, and he was making loud retching sounds. A nurse stated, "This is the second time this week he's been here, he is

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nothing more than a drug seeker. He has been here two or three times every week for the past 3 weeks." His mother was with him, and she appeared concerned and frustrated. She stated, "I want this taken care of this time." A review of his medical records indicated that the last time he was seen in the emergency department he was admitted as an inpatient with abdominal pain and dehydration. He was just discharged the day before yesterday. The diagnosis on the discharge summary was cyclic vomiting syndrome.

While interviewing the patient to obtain a history, he was asked about marijuana use. He stated he smoked some yesterday, four to five joints. He was discharged from the hospital 48 hr prior with no nausea, vomiting, or abdominal pain (he was an inpatient for 48 hr). The provider asked his mother whether she was aware that he has been smoking marijuana, and she informed me that she was the person who purchasing the marijuana (illegally) to help him with his nausea and vomiting.

He was afebrile, tachycardic with a heart rate of 130 beats/min, and blood pressure of 110/68 mmHg. Review his physical examination and consider how would provider manage his plan of care?

Physical Examination

General

The patient was pale, diaphoretic, with dry mucous membranes and pale skin.

Skin

Pale and warm to touch; the patient denied itching.

HEENT

PEERL. No fundoscopic abnormalities. Conjunctivae normal. Nose clear without exudates or lesions. Mucous membranes pale and dry. Tongue rugged. Slight erythema in posterior pharynx.

Heart

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No murmurs or rubs.

Lungs

No crackles or abnormal sounds bilaterally.

Abdomen

No guarding or rebound; abdomen soft and nondistended, with normal bowel sounds.

Genitalia/Rectal

Stool in the rectum brown, heme negative.

Musculoskeletal/Extremities

Normal muscle strength in all extremities. Peripheral pulses 2+. The patient denied any tenderness.

Neuro

A and O × 3. No focal weakness. Normal reflexes. Normal coordination and gait.

Laboratory Test Results

The complete blood cell (CBC) count, the chemistry panel, and the amylase and lipase were normal. Liver function tests were also within normal limits.

Pharmacology Of Cannabis

The plant genus Cannabis contains 60 cannabinoids unique to the plant. Delta-9-tetrahydrocannabinol (THC) is the most potent psychoactive agent of the cannabis plant. Other plant cannabinoids are cannabinol and cannabidiol. Cannabinoids are found in the stalks, leaves, flowers, and seeds of the plant and also within the resin of the female plant. Breeding techniques of the cannabis within the past 20 years has increased the potency of the plant. In 1960, a joint

contained about 10 mg of THC, and today a joint contains about 150 mg of THC (Ashton, 2001).

When smoking a joint, 50% of the THC is inhaled, absorbed in the lungs, and rapidly enters the bloodstream with a peak level attained within 2 hr. Cannabis consumed orally reaches blood concentrations of 25%–30% of that obtained from smoking. Onset effect of the oral consumption is delayed by 0.5–2 hr because of the slower absorption from the gut. Absorbed cannabinoids accumulate in the fatty tissues of the body, reaching a peak in 4–5 days. Half-life of THC is 7 days, and complete clearance takes approximately 30 days (Ashton, 2001).

Disease Description and Pathophysiology

Cannabinoid hyperemesis syndrome is a disease caused by the chronic use of cannabis. Consequently, some of the long-term users develop recurrent (cyclic) events of nausea associated with violent vomiting and colicky, cramping, epigastric, abdominal pain. These symptoms may be relieved by taking a hot bath or hot shower; however, when the hot bath or shower is completed, the symptoms return. Three phases of the disease have been identified as the prodromal, hyperemetic, and recovery phases. In the prodromal phase, patients may experience some early morning nausea associated with the sight or smell of foods; there may be some weight loss associated with this phase. There is no compulsive bathing noted during this phase. The hyperemesis phase is when the patient starts to have profuse vomiting with the colicky, epigastric, abdominal pain. It is during this period, the patient learns that the hot baths or showers will help with the symptoms. It is also during this phase the patients will visit the ED for management of the overwhelming vomiting and retching. The recovery phase begins only when cannabis use is stopped (Allen et al., 2004; Galli et al., 2011; Price, Fisher, Kumar, & Hilgesson, 2011; Soriano-Co et al., 2010; Sun & Zimmerman, 2013).

Tetrahydrocannabinol is the key component in cannabis, and it affects the cannabinoid receptor system within the body. The cannabinoid receptor system is involved in the physiological processes of appetite, pain sensation, mood, and memory. Cannabinoid receptor cells identified as cannabinoid receptor 1 (CB1) receptors are located

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mainly in the brain. CB1 receptors are also located within the gastrointestinal system, within the enteric nervous system. The effects of THC are mediated mainly by the CB1 receptors. It is the CB1 receptors within the gastrointestinal tract that have an effect on nausea, vomiting, and gastrointestinal inflammation (Galli et al., 2011). CB2 receptors are located in the gastrointestinal systems as well and only have an immune effect on the body (Galli et al., 2011; Pertwee, 2001). Cannabis slows the motility of the gastrointestinal tract, helping with nausea and vomiting, and is used medicinally for this purpose (Galli et al., 2011).

Pertwee (2001) documented multiple studies conducted with mice, rats, guinea pigs, and humans, showing the effects of THC on the gastrointestinal tract. With prescribed doses of THC, an antiemetic effect was found. However, pretreatment with a cannabinoid prior to the prescribed dose caused a tolerance to the inhibitory effects of the cannabinoid, provoking nausea, vomiting, and abdominal pain (Pertwee, 2001). This may be the effect seen in the case of a chronic marijuana user who exhibits hyperemesis and abdominal pain. Another theory is that the toxicity of the CB1 and CB2 cells occurs from the chronic use of THC (Simonetto et al., 2012)

Cannibidiol (CBD) and cannabigerol (CBG), two other components of cannabis, appear to regulate the antiemetic properties of THC. In animals, it was found that low doses of CBD and CBG had an antiemetic effect on the animal; however, high doses of CBD and CBG lead to vomiting (Galli et al., 2011).

Differentials for Cyclic Vomiting and Diagnostic Criteria

The differentials for cyclic vomiting would include (but are not exclusive to) hyperemesis gravidarum, bulimia, Addison's disease, cyclic vomiting, psychogenic vomiting, or pancreatitis. Diagnostic tests will help differentiate the diagnosis (see Table 1). Reviewing the diagnostic studies of these 116 patients provides guidelines for evaluation of the patients with recurrent vomiting.

Diagnostic criteria reviewed in the research conducted by Allen et al. (2004), Soriano-Co et al. (2010), and Simonetto et al. (2012) are documented in Table 2. The main laboratory tests that were done

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were CBC count, basic chemistry, amylase, and a urine drug screen. Soriano-Co et al. (2010) had eight patients in their study and of these only one showed a leukocytosis on the CBC count. Two patients had hypokalemia. The amylase level was normal for all eight patients. Simonetto et al. (2012) identified 98 patients in their study. All of the patients had a normal CBC count, chemistry, and amylase. Allen et al. (2004) had 10 patients in their study and results of the white blood cell count on the CBC count ranged from 11.5 to 16.9. The basic chemistry showed normal potassium and sodium levels. All 10 patients had negative amylase levels. All 10 patients tested positive for cannabis on the urine drug screen.

Abdominal ultrasonography was done in all of the studies. Simonetto et al. (2012) reported that all of the ultrasonograms showed normal findings. Allen et al. (2004) reported that nine of the 10 patients had abdominal ultrasonograms and all nine showed normal findings. Soriano-Co et al. (2010) found fatty livers in 12.5% of their patients.

Treatment

There is no documented evidence-based protocol for the treatment of CHS. Information in the literature from case studies is used as treatment guidelines (Hickey, Witsil, & Mycyk, 2013; Sun & Zimmerman, 2013). Guidelines to follow initially when treating CHS are to prevent dehydration, correct electrolyte deficiencies, and relieve the nausea, vomiting, and abdominal pain. The patient should be hydrated with a liter of normal saline. Any antiemetic agent can be used for the presenting symptom of nausea and vomiting: ondansetron (Zofran), metoclopramide (Reglan), promethazine (Phenergan) with diphenhydramine (Benadryl), or prochlorperazine (Compazine; Pareek, Fleisher, & Abell, 2007; Wallace, Andrews, Garmany, & Jelley, 2011). Abdominal pain initially can be treated with morphine or hydromorphone (Dilaudid). When the diagnostic test results have returned and ruled out other potential causes of recurrent vomiting and abdominal pain, the persistent symptoms need to be addressed. In most cases of CHS, the diagnostic test results show normal findings (see Table 2). The persistent symptoms now need to be addressed.

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Hickey et al. (2013) identified a patient with CHS in their ED; initially, they treated him with a liter of saline, ondansetron (Zofran) 4 mg intravenously and a single dose of hydromorphone (Dilaudid) for his abdominal pain. All of his diagnostic laboratory results showed normal findings, and his symptoms persisted. It was decided that the patient's symptoms persisted at the same level 1 hr after treatment; therefore, a dose of haloperidol (Haldol) 5 mg intravenously was tried. After reviewing anesthesia literature related to nausea and vomiting postoperatively, it was noted that haloperidol worked; therefore, in this case of CHS, Hickey et al. (2013) tried a dose of haloperidol (Haldol) 5 mg intravenously. Within 1 hr, all of the symptoms subsided and the patient with CHS was discharged home with instructions to stop using marijuana.

Pareek et al. (2007) reviewed literature of case studies related to CHS and determined that treatment of CHS should include either ondansetron (Zofran) 4 mg intravenously or promethazine (Phenergan) 25 mg intravenously with diphenhydramine (Benadryl) 25–50 mg intravenously. If this treatment of nausea and vomiting did not work, it was recommended to use any benzodiazepine to promote sleep, which was found to stop the acute episode of vomiting. The benzodiazepine they identified in their article was lorazepam 1 mg intravenously and it could be repeated every 4 hr as needed. A summary of treatment options for the hyperemetic phase are given in Table 3.

Conclusion

The patient in our case study did receive Zofran (ondansetron) 4 mg intravenously for his nausea and Ativan (lorazepam) 1 mg for his abdominal pain along with a liter of fluid. When the laboratory results were reviewed, the likely cause of symptoms was explained to the patient. It was discussed that when he was an inpatient in the hospital, he was not using marijuana and his symptoms improved; however, when he went home and began smoking marijuana joints, all of the symptoms returned with a higher intensity. His mother then verbalized her understanding of the situation and wanted to better understand why marijuana used for nausea medicinally was not working for her son. Educating patients about recreational and over-

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the-counter medication, effects, and side effects is a key component of discharge teaching.

It is important for advanced practice nurses to be able to identify CHS in their differentials of patients presenting to the ED with recurrent nausea, vomiting, and abdominal pain. They need to be knowledgeable about CHS to provide the proper management of care for this specific medical condition.

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Keywords: cannabinoid hyperemesis; cannabinoid hyperemesis syndrome; hyperemesis; recurrent vomiting

Table 1. Differential diagnoses

Differentials	Symptoms of disease differentiating it from cannabinoid hyperemesis
Hyperemesis gravidarum	Positive pregnancy test
Bulimia	Binging or purging
Addison's disease	Fatigue, hyponatremia, hyperpigmentation, hyperkalemia, hypotension
Cyclic vomiting	Family history of migraines, psychological stressors
Pancreatitis	Elevated amylase level

Table 2. Literature review: diagnostic results for cannabinoid hyperemesis

	Simonetto et al. (2012), *n* = 98 patients	Soriano-Co et al. (2010), *n* = 8 patients	Allen et al. (2004), *n* = 10 patients
CBC count			
WBC count	Normal	1 Leukocytosis	Range = 11.5–16.9
Hemoglobin			
Chemistry	Normal	2 Hypokalemia	Potassium = 3.5 Sodium = 138
Amylase	Normal	Normal	Normal
Urine drug screen	No endoscopy	None done	Positive for cannabis
Endoscopy	None documented	75% mild esophagitis 25% not reported	1 Grade 4 erosions 3 Grade 2 erosions 3 Normal 3 No scope done
Gastric emptying	61 Patients were tested 28 Normal 18 Delayed emptying 15 Rapid emptying	None done	2 Normal 1 Delayed emptying 7 Not done
Colonoscopy	Not done	Not done	5 Negative 5 Not done
Abdominal ultrasonography	Normal	12.5% fatty liver 62.5% normal 25% not reported	9 Normal 1 Not done

Note. CBC = complete blood cell; WBC = white blood cell.

Table 3. Treatment options: hyperemetic phase of cannabinoid hyperemesis syndrome

Agent	Indication and dose
Intravenous normal saline	Hydration: 1–2 Liters as needed
Morphine	Abdominal pain: 4 mg intravenously
Hydromorphone (Dilaudid)	Abdominal pain: 5 mg intravenously Only one dose is given until diagnostic results are received
Ondansetron (Zofran)	Nausea and vomiting: 4 mg intravenously
Metoclopramide (Reglan)	Nausea and vomiting: 10 mg intravenously
Promethazine (Phenergan)	Nausea and vomiting: 25 mg intravenously
Prochlorperazine (Compazine)	Nausea and vomiting: 10 mg intravenously
Haloperidol (Haldol)	Persistent nausea and vomiting: 5 mg intravenously

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