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From Heave to Leave:

Understanding Cyclic Vomiting Syndrome

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Abstract

Cyclic vomiting syndrome (CVS) is an idiopathic functional gastrointestinal disorder that has been underrecognized in the adult population. Nausea, vomiting, and abdominal pain are common presentations to gastrointestinal nursing. There are multiple differential diagnoses the clinician must consider prior to a diagnosis of CVS to recognize the disorder. CVS occurs in 4 phases: (a) interepisodic, (b) prodromal, (c) vomiting, and (d) recovery. Each phase has specific treatment guidelines. There is no specific “cure” for CVS; proper management is key. Increasing awareness of CVS is paramount to its detection. CVS has been examined in the pediatric population and has often been considered a pediatric disorder. More recently, it has come to be recognized in the adult population. Proper care and management of these patients allow for better support for patients and their families who are often on the primary caregivers. Nurses are often on the front lines of care and knowledge of CVS from the beginning should lead to shortened hospital stays and optimal patient care.

Nausea, vomiting, and abdominal pain are common patient symptoms managed by gastrointestinal (GI) nurses. Differential diagnoses are often vast and range from gastroparesis and gastritis to intoxication, which makes these symptoms challenging to treat. Furthermore, another underrecognized entity presenting in this manner is called cyclic vomiting syndrome (CVS). It is an underappreciated idiopathic episodic disorder characterized by recurrent episodes of nausea and vomiting with symptom-free periods in-between.

Background

CVS was first examined by Dr. Samuel Gee in the late 19th century when he reported a series of nine children aged 4 to 8 years (Gee, 1882). CVS has been historically categorized as a childhood disorder, but it is now being recognized as affecting the adult population at increasing rates. It is estimated that 1.6% of children experience CVS symptoms, but the prevalence in adults is not known (Abu-Arafah & Russell, 1995).

CVS is primarily diagnosed through clinical history, physical examination, and fulfillment of Rome III criteria. This criterion is defined as acute episodes of vomiting, three or more episodes in 1 year, and absence of nausea and vomiting (Tack et al., 2006). Recognition of CVS highly impacts patient care and facilitates an appropriate treatment regimen. Many patients incur repeated visits to the emergency department (ED) and undergo hospitalizations without a directed treatment plan. A comprehensive management plan for these patients should be in place and aim to decrease healthcare utilization and improve the overall quality of life of these patients. The aims of this article were to highlight aspects of the history and physical examination relevant to CVS, discuss the overall clinical presentation that might lead a clinician to suspect CVS, and provide guidelines for the diagnostic testing and management of CVS. This article uses a case study for the presentation and management of a typical CVS patient.

Recognizing CVS

Mr. Jones, with a chief complaint of nausea and vomiting, presented to your ED. He was vomiting when he presented to the ED and was told to wait until there was an available bay. Mr. Jones continued to vomit nonstop in the waiting room. A triage nurse asked Mr. Jones how much he had to drink that night. Between retching episodes, Mr. Jones replied, “Drink? I can’t hold anything down.”

His wife stated: “This happens all the time and there doesn’t seem to be rhyme or reason. He has eliminated alcohol and watches what he eats, but we can’t pinpoint why he won’t stop vomiting. He has been very good about taking his hydromorphone when the pain gets bad. He does everything he has been told to do by his providers.”

As the nurse, you were cautious at first but saw the discomfort Mr. Jones displayed and heard his wife’s tone of desperation. Mr. Jones related that he had been experiencing nausea and vomiting episodes for more than 2 years. He reported that in July 2009, he left his position at the time as an accountant to assume a new accounting position at a high-ranked company. He said this was a bittersweet time in his life as he was leaving a position he loved for a position with more power and time commitment, but significantly more compensation. He was preparing for his first day on the job when he noticed some nausea that morning. He chalked it up to first day “butterflies,” but 1 hour later he experienced continuous vomiting. He reported having a cup of coffee and a bagel for breakfast, but this was a typical breakfast for him. He also had loose stools, which resolved a few hours later. He thought when his bowel movements improved, he would stop vomiting, yet he continued to vomit during the day and had to leave only after 2 hours of being in the office. He thought he would go home and rest and be ready for the next day.

He woke up the next day not feeling much better. He thought about eating breakfast but held off for an hour. He then felt more nausea coming on and started to vomit once again. He vomited 10 times that day and finally, at 6:00 p.m., he went to the ED. He was given some intravenous (IV) fluids and IV ondansetron (Zofran), which helped. He was not taking any other medications at the time. He then reported that after his visit to the ED, he felt well. Two days later he again started vomiting and again returned to the ED. This time he was

given ondansetron, IV fluids, and hydromorphone, which was thought to relieve pain from retching. This helped for the next 2 weeks, but Mr. Jones never felt 100% better.

After 2 weeks, he started to feel nauseous and went to the ED immediately. He was again given IV ondansetron and told to make an appointment to see a GI specialist. He saw his local GI provider who gave him Zofran to take when he felt nausea coming on, refilled his hydromorphone, and scheduled his 3 month follow-up. At his 3-month follow-up, Mr. Jones reported he had two brief episodes, but between vomiting episodes, he was feeling much better. He continued to have episodes of vomiting and would be out of commission for 2–5 days but would get relief if he could sleep enough. He lost his job 3 months later and became very frustrated and depressed. He told you he has been miserable for the past 4 months and has been to five different EDs multiple times each in the past 2 years. He pleaded with you to find a cure for his vomiting as he feels much hopelessness at the thought of dealing with this in the future.

Pathophysiology

CVS is essentially an idiopathic disorder. Many have hypothesized causes to explain CVS, but there is no definitive origin. Table 1 reviews a list of differential diagnoses one might consider when presented with a potential patient with CVS. Some associations with CVS include migraines, mitochondrial dysfunction, autonomic dysfunction, and neuroendocrine dysfunction (Sunku, 2009).

The association with migraines and CVS has been well known for longer than a century (Whitney, 1898). Many of the symptoms associated with migraine such as nausea, fatigue, and aura are also seen in CVS. In a study of 39 pediatric and adult subjects with CVS, 38.9% of the pediatric subjects and 23.8% of the adult subjects had the presence of a migraine and/or family history of migraine (Prakash, Staiano, Rothbaum, & Clouse, 2001).

Stress, anxiety, fatigue, and infection are all common problems that may lead to CVS. Namin et al. (2007) found that mental stress was a contributing factor in half their patients surveyed with CVS. These symptoms can contribute to dysfunction of the body's mitochondria, which provide cellular energy. Mitochondrial DNA is derived from the maternal side, and there has been a higher association with migraine on this side as well, which leads one to further suspect a relationship to CVS (Sunku, 2009). The autonomic nervous system controls symptoms of flushing, drooling, pallor, fever, fatigue, and gut dysmotility, which frequently occur in CVS (Sunku, 2009).

One recent retrospective study on CVS was done by Hejazi, Lavenbarg, and McCallum (2010). The aim of the study was to better understand autonomic nerve function in adult patients with CVS. The study involved measurement of the sympathetic and parasympathetic nervous system as well as a 4-hour gastric emptying (GE) study. There were 22 adult subjects with CVS enrolled, of which 43% demonstrated autonomic nerve dysfunction.

There are also elements of neuroendocrine dysfunction associated with CVS. Corticotropin-releasing factor serves primarily to stimulate the anterior pituitary to secrete adrenocorticotrophic hormone, which activates the hypophyseal-pituitary-adrenal axis.

Corticotropin-releasing factor is a brain-gut modulator and released in response to stress. It has been associated with nausea, anorexia, and delayed GE. Corticotropin-releasing factor releases in animals and humans have also found to be parallel (Sunku, 2009).

Your mind raced as you thought of these multiple possibilities. You note that there is no compromise to Mr. Jones' airway and he is breathing at a regular rate. His pulse rate was elevated at 90 beats per minute, but you could tell he was anxious. Some differential diagnoses that came to your mind include gastrointestinal such as peritonitis, appendicitis, cholecystitis, and food poisoning. You do a focused physical examination and send Mr. Jones for a computed tomographic scan of the abdomen to ensure that there is no pathological cause to his vomiting. The computed tomographic result comes back negative and you then consider a second line of more benign diagnoses. These include gastroparesis or GI virus. You then recall hearing about something called cyclic vomiting, but you do not know much about this disorder. Given his severe vomiting, you consult with your physician and nurse practitioner colleagues and decide to further examine the GI system.

Diagnosis

The diagnosis of CVS in the adult has been obscure in the nursing and medical literature. Delay in diagnosis seems to be less frequent in pediatric patients (1.9 years) than in adult patients (7.9 years) (Sunku, 2009). This is likely because of a misunderstanding of the presentation of CVS, making diagnosis difficult. Although CVS is frequently diagnosed in pediatrics, recent evidence suggests that CVS is much more common in adults than previously thought. Adult patients often go undiagnosed for some time because of lack of recognition of the disorder with reports suggesting a delay in diagnosis for up to 8–21 years following disease onset (Abell et al., 2008).

CVS in adults is diagnosed through clinical history and physical examination and is based on the Rome III criteria (Drossman & Dumitrascu, 2006). The Rome III criteria describe CVS as periodic episodes of vomiting with the following characteristics: a sudden or acute onset, duration usually less than 1 week, three or more discrete episodes occurring in the prior year, and absence of symptoms between attacks (Hejazi et al., 2010).

CVS has been difficult to diagnose in the adult population because of the lack of understanding of the disease presentation. Venkatesan et al. (2010) attribute this difficulty in diagnosis and the widely unrecognized status of CVS, especially in adults, to an increase in the use of ED services. Given the problems with diagnosis, CVS is likely more common than currently thought (Drossman & Dumitrascu, 2006).

Misdiagnosis of CVS leads to a 3- to 8-year delay in correct diagnosis in adults and a 2.5-year delay in children (Drossman & Dumitrascu, 2006). Through surveying of ED use in patients with CVS, Venkatesan et al. (2010) conclude that the experiences of CVS patients with acute episodes treated in the ED are suboptimal with delay in recognition, referral, and infrequent use of patient-specific treatment protocols. The lack of understanding of the disorder and its treatment not only increases healthcare costs but also negatively impacts the quality of life of the adult patient.

CVS attacks eminently impact patient quality of life. Fleisher, Gornowicz, Adams, Burch, and Feldman (2005) recently described that 32% of patients in a study of 41 adults experienced a coalescence of attacks severe enough that they were completely disabled and required financial support. Patients also go to extreme measures to alleviate some symptoms. Fleisher et al. (2005) continue to describe 13 patients whose thirst was so strong that they began drinking out of toilets to satisfy thirst or drank a large amount of water that would induce vomiting, which in turn made them feel better.

Gastric emptying scan has been one measure used to rule out gastroparesis that has symptoms similar to those of CVS. One study found that 5% of patients referred to a major medical center for evaluation of gastroparesis had CVS (Abell et al., 2008). Hejazi et al. (2010) best illustrated the impact of GE scan on CVS diagnosis. They studied 92 adult patients (47 of which were male) aged 20–68 years with the diagnosis of CVS between 2003 and 2009. They found that 54 subjects (59%) were shown to have rapid GE transit, 25 (27%) had a normal GE transit, and 13 (14%) had slow GE transit. This study concluded that GE is generally rapid or normal in cyclic vomiting patients. Hejazi and McCallum (2011) also studied autonomic nerve function in CVS and found that 57% of patients had rapid GE; however, this was not consistent with autonomic testing results. As discussed previously, autonomic nerve dysfunction has been seen in 43% of CVS patients, specifically the sympathetic nervous system.

You received Mr. Jones' GE study results, which demonstrated normal emptying at 1 hour, 90 minutes, 2 hours, and 4 hours. You are happy that the finding from the study is normal, but want to understand how you can reduce his symptoms.

The Pattern of CVS

There are essentially two types of vomiting: chronic vomiting and cyclic vomiting (Li, 1993). Chronic vomiting occurs in a daily fashion whereas cyclic vomiting is episodic and volatile. If the patient is vomiting two to three times in an hour every day of the month, one might consider a diagnosis of chronic vomiting. A CVS patient paints a different picture in vomiting 10–14 times per hour two or less times per month. Table 2 offers some specific questions the clinician should be mindful of when evaluating CVS.

Cyclic vomiting syndrome occurs in four phases: (a) interepisodic, (b) prodromal, (c) vomiting, and (d) recovery phase. Figure 1 highlights the tortuous course a patient with CVS might take. The interepisodic phase is defined by a symptom-free period. The prodromal phase is the first sign a patient gets of an incipient attack. These symptoms may include nausea or headache. The vomiting phase occurs when efforts to abort the attack fail, which are further discussed in the Treatment section. The recovery phase occurs once treatment has been effective and the patient is able to stop vomiting and work toward recuperation.

Treatment

Current treatment options for CVS remain rather empiric (Pareek, Fleisher, & Abell, 2007). Treatment management is applied according to the phase the patient is in at the time of presentation. The overall goal to treating patients with CVS is to improve their quality of

life. Unfortunately, there are no specific triggering factors to CVS; however, some patients can identify individual triggers or prodromes they experience prior to an attack. There have been reports of anxiety creating a propensity to an attack, but otherwise CVS is treated on the basis of individual triggers.

Each phase is treated differently; thus, it is important to recognize each phase of the CVS cycle (Pareek et al., 2007). There is prophylactic therapy (taken daily) and acute abortive therapy (taken at first sign of attack and during to break the CVS cycle).

Because the interepisodic phase is a period when the patient is free of symptoms, the patient is treated with prophylaxis medication such as a tricyclic antidepressant (TCA) or selective serotonin reuptake inhibitors. Hejazi et al. (2010) found that 88% of patients with CVS who had been on amitriptyline for a 2-year period reported fewer ED visits and fewer CVS attacks. Boles, Lovett-Barrm, Preston, Li, and Adams (2010) found a 72% efficacy in patients taking prophylactic amitriptyline. Furthermore, 77% of patients in the study taking Co-Q-10 reported higher benefit than side effects, which is even higher than amitriptyline (Boles et al., 2010). Patients should always take one of these medicines every night to help space CVS attacks.

Hejazi, Lavenbarg, Foran, and McCallum (2009) studied 132 CVS patients over 1.6 years and found that 13% of CVS patients did not respond to standard therapy using TCAs such as amitriptyline. They found that migraine headache, psychiatric disorder, chronic narcotic use, and chronic marijuana use are risk factors for recurrent attacks despite high doses of TCAs.

The second phase is the prodromal phase, which occurs almost as a warning of an incipient vomiting attack. The main goal during the prodromal phase is to abort the oncoming vomiting phase with an antiemetic such as Zofran and a benzodiazepine such as ativan. Zofran and ativan can be taken every 4 hours to attempt to break the CVS cycle.

Slusker, Konichzky, and Gothelf (2010) suggest four stages of a biofeedback approach that patients can take to abort an attack. The first is helping patients recognize psychological stressors, for example, understanding the relationship between anxiety and GI symptoms. Second, patients should learn to recognize physiological triggers such as sore throat or heart rate changes that may indicate impending anxiety. Third, patients should learn to change one's mindset or beliefs toward self-efficacy and relaxation (vs. vomiting). Finally, an overall control over mind and body, for example, through breathing exercise techniques, may prevent vomiting episodes.

The vomiting phase occurs if all efforts to quiet the prodromal symptoms fail. Often, it can take patients some time to figure out what inciting event will lead to their cyclic vomiting attack. It is important for the clinician to focus on preventing dehydration and terminate the nausea and vomiting. During this time, medicines such as ativan and Zofran are used every 4–6 hours to allow the patient to sleep and subsequently break the cycle of CVS.

The final phase of CVS is the recovery phase. The patient is often fatigued and somewhat sedated at this point. It is important to allow the patient to rest and fully recover to prevent a relapse of nausea and vomiting. This phase is best managed by giving the patient IV fluids

and medicines to allow for bowel rest. Patients should be brought to the hospital for a three-plus “holiday,” which may allow the body to reset and subsequently break the CVS cycle.

There are no standard treatment protocols for CVS at this time. Treatment is done empirically. Most information on CVS treatment in the literature is based on anecdotal evidence, and what is published has been developed primarily for children. Furthermore, as Table 3 demonstrates, guidelines for adults with CVS have been adapted from pediatric recommendations (Pareek et al., 2007). Clinicians should consider starting a patient on a TCA such as amitriptyline, nortriptyline, or desipramine at a 10-mg dose, titrating up by 10 mg every week depending on the patient’s tolerance.

Another baffling variable in therapy is the incongruity of CVS (Abell et al., 2008). There are multiple subgroups of CVS that include those with migraines, hypertension during episodes, CVS associated with menses, diabetes subgroup, those with coexisting neuromuscular disorders, association with extreme anxiety, morning nausea and/or vomiting only, and postinfectious subgroup (Abell et al., 2008). It is not known whether these different CVS subgroups exhibit different responses to the varied treatments used for the condition (Abell et al., 2008).

Mr. Jones is pleased that his GE scan is normal. His gastroenterologist is not sure what to do next, so he sends Mr. Jones to a specialist in the city, Dr. Cares. Mr. Jones explained his symptoms in great detail to Dr. Cares and Nurse Smith. Mr. Jones expressed how well he felt at times, but when he starts to get nauseous, he knows it will be several days before feeling well. Dr. Cares reviewed all the records and concluded that Mr. Jones’ symptoms are, in fact, consistent with CVS. Dr. Cares explained the four phases of CVS and how important it is to treat prophylactically with a medicine such as amitriptyline, but also have an acute abortive treatment such as lorazepam available to break the cycle.

Nurse Smith then spent an additional 30 minutes with Mr. Jones to ensure that he understood the treatment and provided educational material. The nurse makes sure that Mr. Jones is aware he must take his amitriptyline every night and not skip doses. He will start at 10 mg at bedtime and increase by 10 until he reaches 40 mg. He was instructed to then call the office to report on how he is doing. Common side effects include, but are not limited to, headache, constipation, urinary retention, nausea, and dry mouth. If Mr. Jones tolerates the 40 mg, the dose will then be increased to a 50-mg tablet as a maintenance dose.

Mr. Jones was asked to look for a sign that he might have an attack such as the nausea he described occurring 20 minutes before vomiting. At the first sign of these symptoms, Mr. Jones was instructed to take Zofran 8 mg sublingual and ativan 1 mg sublingual every 4–6 hours as needed to abort the attack. He should also practice deep breathing exercises that he was taught by Nurse Smith to decrease stress, thus making it more likely to abort an attack. If this does not work within 24 hours, he was told to call Dr. Cares’ office and an admission for IV fluids and administration of the medicines will likely be indicated.

Mr. Jones was amazed at all the information he is learning. He wondered why he has not heard of this before. He was grateful for the time the nurse and physician spent with him. If

he tolerates the amitriptyline, he will return in 3 months or sooner to follow up on his progress.

Choung et al. (2012) have found that cannabinoid users were 2.4 times more likely to have CVS than patients with functional vomiting. Choung et al. (2012) define functional vomiting as one or more vomiting episodes per week, with no evidence of an eating disorder, including self-induced vomiting, rumination, major psychiatric illness per DSM-IV, CNS abnormalities, or metabolic issues to explain recurrent vomiting. The causal relationship of marijuana to CVS, however, has yet to be determined.

Conclusions

Cyclic vomiting syndrome continues to be an underrecognized disorder. Increasing healthcare provider awareness of the signs and symptoms of CVS should greatly improve the outcomes of the patients suffering with the disorder. Despite great unknowns that accompany CVS, identifying patients with CVS and applying the current treatment regimens can significantly improve the quality of life of patients and their families who often feel a sense of hopelessness. Further study on CVS is needed to better understand a more definitive etiology, which will lead to the optimal treatment of patients.

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FIGURE 1.

Cyclic vomiting syndrome (CVS) cycle. The figure demonstrates two pathways in the course of CVS. One pathway takes the reader through a typical CVS attack (A). The other path shows the improvement that can be made when a CVS attack is aborted using medicine and hydration therapy (B).

TABLE 1.**Differentials of Cyclic Vomiting Syndrome Symptoms**

Chronic abdominal pain
Chronic intestinal pseudo-obstruction
Dehydration
Endocrine condition
Gastritis
Gastroparesis
Hormonal and metabolic disorder
Intoxication
Mitochondrial disorder
Neurological condition
Pancreatitis
Peptic ulcer disease
Renal disorder
Thyroid condition

TABLE 2.**Is It Cyclic Vomiting Syndrome?**

Take a careful history assessing: How often does vomiting occur? Is there is a complete resolution of symptoms between episodes? Was there an incipient event?
Examine gastrointestinal studies including but not limited to: Gastric emptying scan. Upper endoscopy and colonoscopy. Computed tomographic scan. Small bowel follow-through. Magnetic resonance enterography.
What medicines is the patient taking?

TABLE 3.**Cyclic Vomiting Syndrome Phasic Treatment Options**

Phase	Treatment Timing	Treatment Medications
Interepisodic	Prophylactic (daily use)	First Line: TCA
		• Amitriptyline
		• Nortriptyline
		• Desipramine
		Second-line options: (if TCAs fail)
		• SSRI: citalopram
		• Propranolol
		• Cyproheptadine
		• Imipramine
		• Anticonvulsants: phenobarbital, valproate, carbamazepine
Prodromal and vomiting	Acute (abortive)	• Other options: gabapentin, topiramate, levetiracetam, zonisamide
		• Supplements: l-carnitine, coenzyme Q-10
		Antiemetics
		• Ondansetron
		• Granisetron
		• Grepitant
		Benzodiazapine
		• Lorazepam
		Antimigraine
		• Sumatriptan
		• Frovatriptan
		• Rizatriptan
		• Zolmitriptan
		Antiemetics
		• Ondansetron
		Benzodiazapine/sedatives
		• Lorazepam
		• Chlorpromazine
		• Diphenhydramine
		Analgesics
Recovery		• Ketorolac
		Allow patients to recover without relapse of nausea and vomiting

Note. SSRI = selective serotonin reuptake inhibitor; TCA = tricyclic antidepressants