

Positive outcome of administering palonosetron and haloperidol combination in cyclic vomiting syndrome: a case report.

S M Sahad Bin Mahmud^{1*} , Mahia Sultana¹ 

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ABSTRACT

Background: Cyclic vomiting syndrome (CVS) is a rare disorder in which a patient suffers from recurrent episodes of nausea and vomiting. Onset usually occurs early in childhood, later it might progress into a chronic condition highly affecting on the quality of life. No solid treatment protocol is available to treat CVS. There are many cases in which no improvements are observed after years of trying different treatment regimens.

Case Presentation: Here we report a 15-year-old female who was diagnosed as a patient of CVS at the age of 7. She was admitted to the medicine ward within 3 hours of onset in the last year. The patient possesses a history of a unique pattern of onset. She has been hit by the recurrence of the disorder almost once in 8-11 months, lasting for 10-14 days, manifesting as intense nausea, and vomiting once in every 20-40 minutes followed by irregular asymptomatic intervals. Various treatment regimens of unsatisfactory outcome were applied on this patient over the years. After analyzing her previous treatment protocols, we decided to try something new and aggressive, moving with palonosetron and haloperidol, a combination that was never applied on this patient.

Conclusion: The outcome was 'magical' according to the parents of the patient marked by declining of the symptom immediately and complete relief within the next 72 hours, the earliest ever after having onset for this particular patient's past history of encountering CVS.

Keywords: 5-HT3 antagonist, typical antipsychotic, palonosetron, haloperidol, cyclic vomiting syndrome, case report.

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Correspondence to: S. M. Sahad Bin Mahmud

*Department of Internal Medicine, Khulna Medical College Hospital, Khulna, Bangladesh.

Email: dr.sahad@hotmail.com

Full list of author information is available at the end of the article.

Background

Cyclic vomiting syndrome (CVS) is a relatively rare gastrointestinal disorder characterized by episodic nausea and vomiting. Average age of onset is 5 years, females are more prone to CVS than males [1]. Exact etiology is not understood but psychological stress acts as one of the very few important trigger factors. Motion sickness, sleep deprivation, migraine, menstruation, and even certain dairy food products could be the other triggers [2]. CVS may or may not be associated with other symptoms such as abdominal pain. It remains as a clinical diagnosis which is based on the following three main criteria (known as ROME III Consensus): stereotypical episodes of vomiting regarding acute onset and duration (<1 week), three or more discrete vomiting episodes in the previous year, and absence of nausea and vomiting between episodes [3,4]. However, longer duration of episodes (>1 week) has been found in some patients with CVS [5]. Physical examination and lab tests can be performed to exclude other possible conditions. No definitive therapy has been proven to be effective for CVS. However, several supportive

as well as experimental treatments has been effective in many cases [6]. Treatment regimen generally includes avoidance of possible triggers and medications such as anti-emetics and sedatives.

Case Presentation

In July 2021, a 15-year-old female patient was admitted in the medicine ward with complaints of periodic vomiting once in every 20 minutes continuing for last 3 hours. We were informed that she was already diagnosed as a patient of CVS at the age of 7, by a renowned gastroenterologist in the city. Coincidentally, the patient started her primary school education that year. Since then, she had experienced multiple recurrence of the condition almost in every year with having exceptions in 2015 and 2016 (Table 1).

Her age of menarche was 12, menstrual cycle was regular, flow was average. Although the patient was admitted as a known case of CVS, to maintain protocol, we performed few physical and laboratory examinations. Her vital signs were normal. No abnormality was detected in

Table 1. Timeline of recurrences.

INSTANCES OF CVS ATTACK	AGE (YEARS)	ANTIEMETICS	RECURRED WITHIN...(MONTHS)	SYMPTOMS LASTED FOR ... (DAYS)
1st	2013	7	(Diagnosed for the first time)	19
2nd	2014	8	10	16
-	2015	9	(Did not have an attack)	-
-	2016	10	(Did not have an attack)	-
3rd	2017	11	33	14
4th	2018	12	09	10
5th	2019	13	08	12
6th	2020	14	09	12
7th	2021	15	09	03
8th	2022	16	11	03

The bold rows in table, highlight the greater effect of palonosetron and haloperidol combination on the duration of symptoms.

Table 2. Record of treatment regimens.

INSTANCES OF CVS ATTACK	AGE (YEARS)	ANTIEMETICS	SEDATIVES	SYMPTOMS LASTED FOR ... (DAYS)
1 st	7	Oral domperidone	Oral cyproheptadine (sedating 1st gen anti histamine)	19
2 nd	8	Oral domperidone	Oral cyproheptadine (sedating 1st gen anti histamine)	14
3 rd	11	Oral ondansetron	Oral amitriptyline (TCA)	14
4 th	12	Oral ondansetron	Oral amitriptyline (TCA)	10
5 th	13	IV ondansetron	Oral diazepam (Benzodiazepine sedative)	12
6 th	14	IV ondansetron	IM diazepam (Benzodiazepine sedative)	12
7th	15	IV palonosetron	IM haloperidol (Typical antipsychotic)	03
8th	16	IV palonosetron	IM haloperidol (Typical antipsychotic)	03

The bold rows in table, highlight the greater effect of palonosetron and haloperidol combination on the duration of symptoms.

Table 3. Medications, order on admission.

DRUGS	ROUTE	DOSAGE		TOTAL NUMBER OF DOSAGES GIVEN
Palonosetron	IV	0.075 mcg/ampule	1 ampule once daily, in the morning	3 dosages (in 3 consecutive days)
Haloperidol	IM	5 mg/ml/ampule	1 ampule once daily, in the evening	3 dosages (in 3 consecutive days)
Esomeprazole	IV	20 mg/vial	1 vial twice daily, morning & evening	6 dosages (in 3 consecutive days)

physical examination. Abdominal X-Ray, ultrasonogram of whole abdomen, and routine biochemical reports were also clear of any abnormality. Patient had no family history of CVS or any other significant illness such as migraine.

We analyzed all the prescriptions issued at previous six instances of CVS attack. Treatment protocols applied on the patient were variable over the years (Table 2). Upon the request by the parents of the patient, who were very much concerned about their child’s upcoming examination in school, we decided to try something different as

well as aggressive as compared to the previous treatments. As anti-emetic, we opted to go with palonosetron which is commonly used for the treatment of chemotherapy-induced nausea and vomiting. For sedation, we chose to administer haloperidol, a butyrophenone drug which also has a role in treating nausea and vomiting. As dosages were concerned, we followed standard protocol (Table 3). Along with this, we kept the patient Nil per os (NPO) and started parental fluid infusion with 2 L of 5% Dextrose saline daily to maintain hydration.

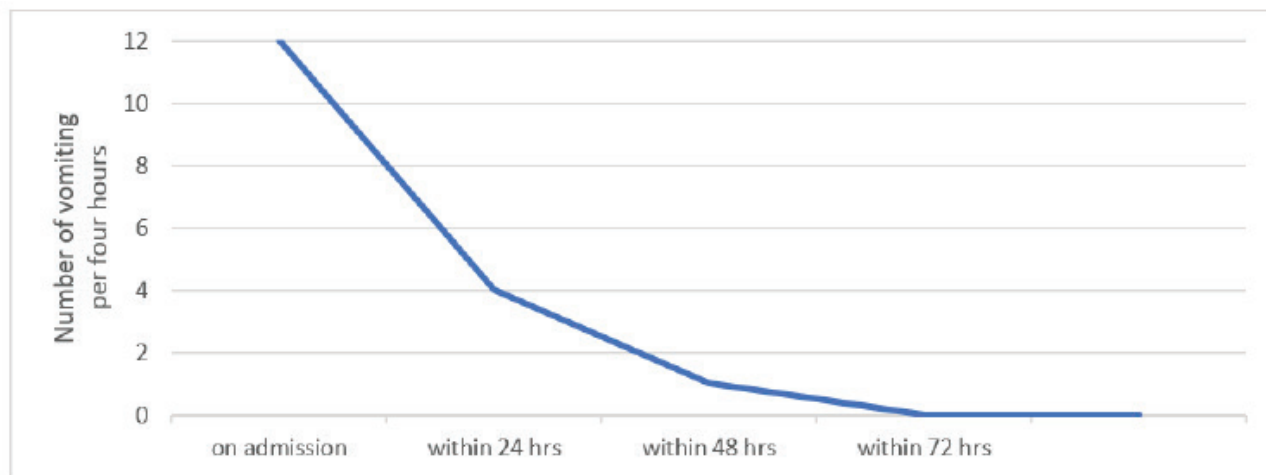


Figure 1. Frequency of vomiting (per 4 hours).

Table 4. Medications, prescribed on discharge.

DRUGS	ROUTE	DOSAGE	DURATION	
Palonosetron	PO	0.5 mg tablet	1 tablet daily, in the morning	7 days
Haloperidol	PO	2.5 mg tablet	1 tablet daily, in the evening	14 days
Esomeprazole	PO	20 mg tablet	1 tablet twice daily, morning & evening	7 days

In a span of 24 hours, we achieved significant result. The frequency of the vomiting started reducing sharply (Figure 1). The patient experienced complete disappearance of symptom within 72 hours which was by far the shortest instance of CVS attack experienced by the patient till date. On discharge, we resumed her diet per oral and continued with oral palonosetron and haloperidol for another few days (Table 4). On 15 days follow-up, the patient was completely well appeared without any further report of vomiting episode. Eleven months later, in June 2022, the patient was again brought to the hospital with episodes of periodic vomiting and was again successfully treated with the same treatment regimen we followed last year.

Discussion

Upon questionnaire, we discovered that, due to a heavy financial crisis in the family, the patient was forced to skip schooling in those 2 years mentioned above in which the condition did not recur. This information makes strong evidence that psychological stress due to burden of study has been an important trigger of CVS for this particular case. Regarding the latest treatment regimen of the patient, palonosetron is a powerful selective serotonin 5-HT₃ receptor antagonist. The antiemetic activity of the drug occurs through the inhibition of 5-HT₃ receptors present both centrally (medullary chemoreceptor zone) and peripherally (GI tract). This inhibition of 5-HT₃ receptors in turn inhibits the visceral afferent stimulation of the vomiting center. On the other hand, haloperidol acts as an antagonist

at dopamine receptors which is an important neurotransmitter at the vomiting center in the brain.

To our knowledge, this case report is the first in which the combination of these two medications has been applied. In this case, the therapeutic outcome was signified by two measures: immediate decline of the frequency of vomiting and cessation of the vomiting phase within 72 hours which was more than 10 days in all previous instances. No particular adverse effect of these two drugs was complained by the patient.

Conclusion

Different therapeutic modules were tried upon the patient over the years. All of those were of unsatisfactory outcomes before the patient finally being responsive to the combination of palonosetron and haloperidol. Having a similar therapeutic outcome in two consecutive years, we believe, this combination could be a highly effective option to treat the vomiting phase of CVS.

What is new?

Different therapeutic modules were tried upon a patient with CVS. All of those were of unsatisfactory outcomes before the patient finally being responsive to the combination of palonosetron and haloperidol. Having a similar therapeutic outcome in two consecutive years, the authors believe, this combination could be a highly effective option to treat the vomiting phase of CVS.

List of Abbreviations

5-HT	5-hydroxytryptamine
GI	Gastrointestinal
IV, IM, PO	Intravenous, Intramuscular, Per oral
NPO	Nil per os (Latin abbreviation for “nothing by mouth”)
TCA	Tricyclic Antidepressants

Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this case Report.

Funding

None.

Consent for publication

Written informed consent was taken from the family of the patient.

Ethical approval

Ethical approval is not required at our institution to publish an anonymous case report.

Author details

S. M. Sahad Bin Mahmud¹, Mahia Sultana¹
 Department of Internal Medicine, Khulna Medical College Hospital, Khulna, Bangladesh

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Summary of the case

1	Patient (Gender, Age)	Female, 15 years.
2	Final diagnosis	CVS.
3	Symptoms	Periodic vomiting once in every 20 minutes.
4	Medications	Palonosetron, haloperidol and esomeprazole.
5	Clinical procedure	Abdominal X-Ray and ultrasonogram of whole abdomen.
6	Specialty	Gastroenterology/Pediatrics/Pediatric Gastroenterology.