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Mary Smith
Clinical Support Librarian  mary.smith30@nhs.net

SUMMARY
Management of CVS includes addressing lifestyle modifications and comorbidities, especially anxiety. Lifestyle modifications to reduce the risk of inducing an attack include adequate fluid intake, avoidance of fasting, using long-acting caloric snacks, good sleep hygiene, and regular exercise. Recognized precipitating factors should be avoided whenever feasible. In children, common triggers include physical exhaustion from lack of sleep, stressors such as bullying at school, motion (car rides, amusement park rides), fasting, and certain foods (eg, chocolate, cheese, cow's milk). In adults, precipitating factors are somewhat less common than in children but may include sleep disruptors (shift work, extended travel across time zones) and psychological stressors related to interpersonal conflict at work or home. If there is a history or prolonged and frequent cannabis use, total abstention can clarify whether this is cannabis hyperemesis syndrome (CHS) or CVS. Management should address comorbid conditions as well. First among them is anxiety, panic attacks, or depression, which are present in 30 to 50 percent of children or adults with CVS. Referral to a medical psychologist for cognitive behavioral therapy is an integral part of our treatment plan, and behavioral intervention can result in marked improvement and reduced school absenteeism and functional disability. In more severe cases, the addition of anxiolytic agents (eg, citalopram, sertraline) may be necessary. If school absenteeism fails to
respond to a graded school-reentry plan, a comprehensive biobehavioral rehabilitation program may be needed for recovery.

Specific interventions depend on age of patient, severity of symptoms, timing of presentation, and setting. Our general approach is as follows •**Prodromal and early symptoms (home management)** – For patients with an episode of CVS that can be identified during the prodrome or shortly after the vomiting begins, we suggest treatment with an abortive agent such as intranasal or subcutaneous sumatriptan or oral aprepitant (Grade 2C). The choice between these options is based largely on patient and provider preference (table 4B). Aprepitant is particularly appropriate for patients without a personal or family history of migraine and those who have failed to respond to triptans. Abortive treatments are most effective if they are given early in the prodrome and should be prescribed to have at home for timely use by the patient. Some patients may have sufficient response to abortive therapy to obviate the need for additional intervention.

•**Acute vomiting episodes (emergency department management)** – For patients who present to the emergency department with moderate to severe vomiting episodes, supportive care includes the following:

- Intravenous hydration – Intravenous fluids should be given to replace fluid losses. Hypovolemia is initially corrected with fluid boluses (eg, 10 to 20 mL/kg of isotonic saline). For ongoing maintenance fluid therapy in children, we suggest a half-normal saline (0.45% sodium chloride) with 10% dextrose rather than lower dextrose concentrations. For adults, we typically use isotonic saline (0.9% sodium chloride) with 5% dextrose. This dextrose infusion may lessen the catabolic state and ketosis induced by the acute CVS episode, which can prolong vomiting.

- Antiemetic therapy – For patients presenting with acute vomiting episodes, we suggest initial treatment with high-dose 5-hydroxytryptamine (5-HT₃) receptor antagonist (eg, ondansetron, granisetron). In addition, we suggest concomitant treatment with a sedative medication (eg, diphenhydramine or lorazepam). The sedative medication provides additional symptom relief, which is valuable because control of nausea and vomiting is often incomplete with 5-HT₃ receptor antagonist therapy. Triptan therapy (eg, sumatriptan) may be useful if the patient presents to the emergency department in the very early phases of the episode (ie, within one hour of the onset of vomiting), but this is rarely the case.

**Environmental measures** – Whenever possible, the patient should be kept in a dark, quiet, low-stimulation environment because any disturbance of the hyperesthetic patient typically incites more nausea and vomiting.

**Treatment of pain** (if present) - Management of abdominal and headache pain usually begins with an intravenous nonsteroidal antiinflammatory drug (eg, ketorolac). If the pain has a midepigastric or dyspeptic quality, an antireflux medication (eg, histamine type 2 receptor antagonist or proton pump inhibitor) is a reasonable adjunctive therapy. Narcotics are reserved for severe and refractory pain since they can worsen vomiting and induce dependence over time.

•**Prophylactic therapy** – For patients who experience CVS episodes that are frequent, prolonged, or debilitating, or that result in recurrent emergency department or hospital admissions, we suggest prophylactic therapy. The limited evidence for the use of these medications for CVS suggests similar levels of efficacy, so selection among these
medications is based primarily upon side effects and toxicities, as well as differences in the amount of clinical experience with use of each drug for CVS within each age group.

**Children <5 years** - we suggest prophylactic treatment with cyproheptadine or pizotifen rather than other agents. This preference is based primarily on a more favorable side effect profile in younger children and is supported by an expert panel. Potential side effects of cyproheptadine include weight gain and sedation.

**Children ≥5 years and adults**, we (and an expert panel) suggest amitriptyline or other tricyclic antidepressant. This preference is based upon the greater clinical experience with amitriptyline for CVS compared with alternative agents (aprepitant, topiramate) and overall higher level of effectiveness, despite frequent but tolerable side effects. Alternatives include aprepitant, propranolol (typically used only for children), or selected anticonvulsants. In addition, for most children who warrant prophylaxis, we suggest a trial of concomitant treatment with coenzyme Q10, with or without L-carnitine and riboflavin supplementation. Coenzyme Q10, sometimes with riboflavin, is sometimes used as an adjunct to other prophylactic agents in adults, based upon indirect and very limited evidence for efficacy in prophylaxis of migraines. [This summary was provided by UpToDate®]

Very little was found from the literature search on psychological approaches to CVS

- A small case series found that therapeutic management with a focus on behavioural modification, adaptive coping skills, and a healthy therapeutic relationship was found to be efficacious in gradually remitting this condition [1]
- HRQoL for families was associated with anxiety symptoms to a greater extent than disease characteristics, indexing the importance of a biopsychosocial approach to CVS management. Screening for anxiety symptoms and support for school absences due to illness are indicated to help lessen the impact of CVS on the family as a whole. [5]
- Psychological interventions commonly used are cognitive behavior therapy (CBT), relaxation techniques such as progressive muscle relaxation technique, guided imagery, and rarely hypnosis [10]

**SEARCH RESULTS**

Cochrane Central Register of Controlled Trials: Effects of an Integrative Health Care Model With Meditation and Care Coordination in CVS, April 2020

1. Psychological Intervention in Cyclic Vomiting Syndrome in Adolescents: A Case Series
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   - 1 Department of Clinical Psychology, National Institute of Mental Health and Neurosciences, Bengaluru, India.
   - 2 Department of Clinical Psychology, Dr Ram Manohar Lohia Hospital, New Delhi, India.
   PMID: 31805841
   DOI: 10.2989/17280583.2019.1674660
   Abstract
**Objective:** Cyclic vomiting syndrome (CVS) is difficult to diagnose, thus there is often a delay in diagnosis or a misdiagnosis. In the absence of an adequate understanding of the pathophysiology of the syndrome, it is under-recognised and treatment is difficult. The present case series aimed to assess and manage three adolescents with CVS.

**Method:** The Children’s Apperception Test was administered on the three Asian adolescents who were referred for the management of CVS to the Department of Clinical Psychology at a tertiary care hospital in New Delhi, India. A treatment module was developed to treat CVS in these adolescents.

**Results:** A strong link was found between the psychological stressors and their physical manifestations in the episodes of vomiting. Therapeutic management with a focus on behavioural modification, adaptive coping skills, and a healthy therapeutic relationship was found to be efficacious in gradually remitting this condition.

**Conclusions:** Thus, the focus of treatment in cases of CVS should be to understand the psychological underpinning and help the adolescents to incorporate healthy coping strategies.

**Publication types**
- Case Reports

2. [Cyclic Vomiting Syndrome: An Overview for Clinicians](https://link.to/article)


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   **PMID:** 31702939
   **DOI:** [10.1080/17474124.2019.1691527](https://doi.org/10.1080/17474124.2019.1691527)

   **Abstract**

   **Introduction:** Cyclic vomiting syndrome (CVS) is an under recognized entity causing significant impact on patient’s lifestyle. CVS is characterized by recurrent episodes of abdominal pain, nausea, and vomiting leading to many emergency department presentations prior to diagnosis. Patients often have lengthy delays in starting appropriate therapy leading to significant physical and financial hardship. Most cases of cyclic vomiting syndrome are reversible by managing risk factors and starting on appropriate treatment.

   **Areas covered:** This review covers the diagnostic criteria, pathophysiology, risk factors, and treatment for CVS and provides a valuable resource for clinicians to review and help with managing this challenging syndrome. The latest literature regarding the diagnosis and management of CVS is summarized.

   **Expert Opinion:** The direction for future research in CVS and insights to managing CVS are summarized. The role of pain that can be frequently controlled by tricyclic antidepressants and lorazepam suggests a central nervous system (CNS) origin. A standardized treatment regimen for CVS must be implemented as patients do respond to current therapies but there is often a significant delay in initiation of treatment. Reviewed recent data looking at MRI brain changes in patients with CVS that may lead to a better understanding of the pathophysiology of this disease.

   **Keywords:** Cyclic vomiting syndrome; abdominal pain; functional GI disorders; nausea; vomiting.

3. [Acute Management of Pediatric Cyclic Vomiting Syndrome: A Systematic Review](https://link.to/article)

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PMID: 31540764
DOI: 10.1016/j.jpeds.2019.06.057

Abstract
Objectives: To synthesize quantitative and qualitative data on pharmacologic interventions of pediatric cyclic vomiting syndrome and their effectiveness in disease management in the acute care setting.

Study design: Using keywords, 799 studies published up from December 1954 to February 2018 were extracted from MEDLINE via Pubmed, Embase via OVID, CINAHL via EBSCO, and Cochrane Controlled Trials Registry. Studies were evaluated for inclusion and exclusion by 2 independent reviewers using predetermined inclusion and exclusion criteria.

Results: The search yielded 84 studies for full review, of which 54 were included in the systematic review. Studies were subsequently separated into 1 group of 6 case series studies containing quantitative data on sumatriptan, ondansetron, phenothiazines, prokinetic agents, carbohydrate, isometheptene, and aprepitant; 1 one group consisting only of qualitative studies containing expert recommendations.

Conclusions: Ondansetron has the most quantitative and qualitative evidence to support its inclusion in pediatric emergency department protocols as a rescue therapy. Sumatriptan and aprepitant are potential candidates for inclusion as abortive therapies. Qualitative data from retrospective studies and case reports are not applicable to a larger patient population. This report informs a need for controlled, prospective cohort studies and randomized, controlled trials to optimize current management protocols and to develop new medical interventions.

Keywords: cyclic vomiting; emesis; migraine; pediatric emergency; pharmacologic intervention.

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Publication types
• Systematic Review

4. Managing Cyclic Vomiting Syndrome in Children: Beyond the Guidelines Free PMC article


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PMID: 30076469
PMCID: PMC6153591
DOI: 10.1007/s00431-018-3218-7

Abstract
Cyclic vomiting syndrome (CVS) in children is characterized by frequent hospitalizations, multiple comorbidities, and poor quality of life. In the absence of robust data, the treatment of CVS
remains largely empiric starting with the 2008 NASPGHAN Consensus Statement recommendations of cyproheptadine for children < 5 years of age and amitriptyline for those ≥ 5 years with propranolol serving as the second-line agent. Comprehensive management begins with lifestyle alterations, and extends to medications, supplements, and stress reduction therapies. Standard drug therapy is organized by the four phases of the illness: (1) interictal (preventative medications and mitochondrial supplements), (2) prodromal (abortive agents), (3) vomiting (fluids/energy substrates, antiemetics, analgesics, and sedatives) and (4) recovery (supportive care and nutrition). Because the response to treatment is heterogeneous, clinicians often trial several different preventative strategies including NK1 antagonists, cautious titration of amitriptyline to higher doses, anticonvulsants, Ca^{2+}-channel blockers, and other TCA antidepressants. When the child remains refractory to treatment, reconsideration of possible missed diagnoses and further mono- or combination therapy and psychotherapy can be guided by accompanying comorbidities (especially anxiety), specific subphenotype, and when available, genotype. For hospital intervention, IV fluids with 10% dextrose, antiemetics, and analgesics can lessen symptoms while effective sedation in some instances can truncate severe episodes.

**Conclusion:** Although management of CVS remains challenging to the clinician, approaches based upon recent literature and accumulated experience with subgroups of patients has led to improved treatment of the refractory and hospitalized patient. What is Known: • Cyclic vomiting syndrome is a complex disorder that remains challenging to manage. • Previous therapy has been guided by the NASPGHAN Consensus Statement of 2008. What is New: • New prophylactic approaches include NK1 antagonists and higher dosages of amitriptyline. • Strategies based upon comorbidities and subphenotype are helpful in refractory patients.

**Keywords:** Abdominal migraine; Cyclic vomiting syndrome; Postural orthostatic tachycardia syndrome.

**Conflict of interest statement**

The author declares that there is no conflict of interest.

- **Cited by 1 article**
- **32 references**

**Publication types**

- Review

5. **Family Health-related Quality of Life in Pediatric Cyclic Vomiting Syndrome**


**Authors**

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**PMID:** 29697487

**DOI:** 10.1097/MPG.0000000000001797

**Abstract**

**Objective:** The aim of the study was to evaluate the relationship of disease characteristics and child anxiety symptoms to family health-related quality of life (FHRQoL) in youth with cyclic vomiting syndrome (CVS).

**Methods:** Forty-two parents of youth ages 8 to 18 years diagnosed with CVS completed the Family Impact Module of the PedsQL, a measure of the impact of the child’s illness on the family. We evaluated the relationship of disease characteristics and child and parent proxy
reports of anxiety symptoms on the Screen for Childhood Anxiety and Related Emotional Disorders to FHRQoL.

**Results:** Parent report of child anxiety symptoms and missed school days (mean = 11.93, standard deviation = 14.62) were the strongest predictors of FHRQoL ($r = 0.33$, $df = 1.39$, $F = 8.51$, $P = 0.006$). Other disease characteristics, including frequency, duration, chronicity of CVS episodes, and delay in initial CVS diagnosis were not significantly associated with the FHRQoL total score. Child anxiety symptoms by either parent and/or child report were associated with subscales of the FHRQoL, including family physical functioning, family communication, and family daily activities.

**Conclusions:** HRQoL for the families assessed in this study was associated with anxiety symptoms to a greater extent than disease characteristics, indexing the importance of a biopsychosocial approach to CVS management. Screening for anxiety symptoms and support for school absences due to illness are indicated to help lessen the impact of CVS on the family as a whole.

6. **An Overview of the Clinical Management of Cyclic Vomiting Syndrome in Childhood**

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**PMID:** 29484898
**DOI:** 10.1080/03007995.2018.1445983

**Abstract**
This narrative review provides an update on cyclic vomiting syndrome pathogenesis, diagnosis and management, based upon studies published after the 2008 North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) official recommendations. The review began with a comprehensive PubMed/Medline search for "cyclic vomiting syndrome", "periodic syndromes" and "pediatrics" from 2000 up to October 2017. Additional papers were identified by reviewing the reference lists of retrieved publications. Cyclic vomiting syndrome is a severe, debilitating disorder of the brain-gut axis with unclear pathogenesis, that significantly affects long-term quality of life of affected children and their families. The 2008 NASPGHAN recommendations defined the major clinical, diagnostic and therapeutic peculiarities. Over the last 10 years, advancements in pathogenesis and diagnostic criteria have been made, and new prophylactic and therapeutic strategies have been proposed. These aspects are discussed in this manuscript. For the pediatrician, the major aim is to have early clinical suspicion to avoid diagnostic delay and to start adequate, phase-related, symptom-tailored management.

**Keywords:** Cyclic vomiting syndrome (CVS); diagnosis; management; pediatrics; review.

7. **Cyclic Vomiting Syndrome in Children**

**Authors**
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**Affiliations**
Abstract

Purpose of review: Cyclic vomiting syndrome (CVS) is a misrecognized and probably underdiagnosed episodic syndrome associated with migraine, occurring preferentially in childhood. Attacks are stereotyped for each individual, with predictable periodicity. This review summarizes recent clinical and paraclinical observations in this syndrome, and current approaches in explorations and therapeutics.

Recent findings: Clinical phenotype during prodromal, vomiting, and recovery phases contains visceral and neuropsychological symptoms, but also cranial and systemic symptoms. Some clinical arguments as circadian or circannual periodicity suggest a chronobiological disease. Red flags in clinical presentation are proposed to distinguish other etiologies of recurrent gastrointestinal disturbances and guide paraclinical explorations. Functional magnetic resonance imaging in both CVS and migraine displayed diminished insular connectivity with the sensorimotor network, suggesting a common pathophysiology. Pathophysiology of CVS is not well defined, and there is probably a multifactorial origin. Distinction with other differential diagnoses is a challenge for clinicians. Further research, in particular with functional imaging, are required to define pathophysiology of CVS. Control trials are missing in pediatric population. Injectable or intranasal sumatriptan are often effective. For prophylaxis, amitriptyline, cyproheptadine, or propranolol are the most common treatments, depending on age and comorbidities. Non-pharmacologic measures as lifestyle modification also seem to be effective as preventive treatment.

Keywords: Children; Cyclic vomiting syndrome; Migraine.

43 references

Publication types

Review
pathophysiology as suggested by several studies. Since there are no specific biomarkers available for this disorder, physicians should rely on Rome criteria for the diagnosis. Due to the lack of randomized control trials, the treatment of CVS is primarily empirical.

Comment in
- *Cyclic vomiting syndrome: the nervous system has the guts.*
- Cited by 4 articles
- 45 references

Publication types
- Review

9. *Prophylactic Therapy of Cyclic Vomiting Syndrome in Children: Comparison of Amitriptyline and Cyproheptadine: A Randomized Clinical Trial*
  Authors
  Negin Badihian 1, Hossein Saneian 2, Shervin Badihian 2 3, Omid Yaghini 2
  Affiliations
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  3 Students' Research Center, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran.
  PMID: 28719594 DOI: 10.1038/ajg.2017.194
  Abstract
  **Objectives:** Cyclic vomiting syndrome (CVS) is a common functional gastrointestinal disorder characterized by recurrent episodes of nausea and vomiting. There is no definite treatment for the condition, although some medications are recommended. We aimed to compare the efficacy of amitriptyline and cyproheptadine in prophylactic therapy of CVS.
  **Methods:** This is a single-blinded randomized clinical trial conducted during 2015-2016 in Isfahan, Iran. Sixty-four children who were 3-15 years old, with a diagnosis of CVS (based on Rome III criteria), were included in the study and were randomly divided into two groups of amitriptyline and cyproheptadine. They were followed for 6 months, looking for frequency and duration of attacks as the primary outcome.
  **Results:** The mean monthly frequency of attacks in the last 2 months of the study in the amitriptyline and cyproheptadine group were 0.38±0.55 and 0.59±0.71, respectively (P-value=0.197), after intervention. The mean duration of attacks between amitriptyline and cyproheptadine group were 1.41±2.86 and 1.81±2.22 h, respectively (P-value=0.212). In the amitriptyline group 65.6% of patients reported 100% remission, whereas in the cyproheptadine group 50% reported full remission (P-value=0.206).
  **Conclusions:** There was no superiority of one of the medications over the other. We did not find any age-related effect on the efficacy of these medications as well.
  Comment in
  - *Cyclic Vomiting Syndrome: Randomized Controlled Trials Are also Needed in Adults.*
  - Cited by 7 articles
10. **Cyclical Vomiting Syndrome: Psychiatrist's View Point** Free PMC article


**Authors**

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**PMID:** 28852251

**PMCID:** PMC5560005

**DOI:** 10.4103/0253-7176.211755

**Abstract**

Cyclical vomiting syndrome (CVS) is an idiopathic functional disorder characterized by recurrent episodes of nausea and vomiting separated by symptom-free intervals. Even though initially described in children, it is seen in all age groups. Exact etiology is not known. Various physical, infectious, and psychosocial stressors have been implicated for CVS. High incidence of psychiatric comorbidities such as panic attacks, anxiety disorder, and depression is seen in CVS. Most children outgrow CVS with time though some may transition to migraine or continue to have CVS as adults. Frequent misdiagnosis, delay in diagnosis, or inadequate treatment often lead to years of recurrent vomiting. This case report highlights the importance of the management of CVS by a multidisciplinary team including a psychiatrist in addressing the various physical and psychological factors effectively and that would result in faster and prolonged recovery.

**Keywords:** Cyclical vomiting syndrome; psychological interventions; somatoform disorder.

**Conflict of interest statement**

There are no conflicts of interest.

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11. **Cannabinoid Hyperemesis and the Cyclic Vomiting Syndrome in Adults: Recognition, Diagnosis, Acute and Long-Term Treatment** Free PMC article


**Authors**

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- ² Department of Internal Medicine, General Hospital Luebecke-Rahden, Rahden, Germany.
- ³ Department of Internal Medicine, General Hospital Luebecke-Rahden, Rahden, Germany; Justus-Liebig-University Giessen, Germany.
The cannabinoid hyperemesis syndrome (CHS) and the cyclic vomiting syndrome in adults (CVS) are both characterized by recurrent episodes of heavy nausea, vomiting and frequently abdominal pain. Both syndromes are barely known among physicians. Literature is inconsistent concerning clinical features which enable differentiation between CVS and CHS. We performed a literature review using the LIVIVO search portal for life sciences to develop a pragmatic approach towards these two syndromes. Our findings indicate that complete and persistent resolution of all symptoms of the disease following cannabis cessation is the only reliable criterion applicable to distinguish CHS from CVS. Psychiatric comorbidities (e.g. panic attacks, depression), history of migraine attacks and rapid gastric emptying may serve as supportive criteria for the diagnosis of CVS. Compulsive bathing behaviour, a clinical observation previously attributed only to CHS patients is equally present in CVS patients. Long-term follow-up is essential in order to clearly separate CHS from CVS. However, long-term follow-up of CVS and CHS cases is seldom. We provide a standard operating procedure applicable to a broad spectrum of health care facilities which addresses the major issues of CVS and CHS: awareness, diagnosis, treatment, and follow-up.

Keywords: abdominal pain; cannabinoid hyperemesis; cannabis; cyclic vomiting in adults; hot showering/hot bathing; nausea; periodic vomiting; vomiting.

Conflict of interest statement
The authors declare that they have no competing interests.
Children (TSST-C) in adolescents. 38 subjects (26 females) were enrolled: 11 cyclic vomiting syndrome (CVS), 11 anxiety, and 16 controls. Salivary cortisol, α-amylase and heart rate variability (HRV) were assessed during the TSST-C. Anxiety was measured by the Screen for Childhood Anxiety Related Emotional Disorders (SCARED), Anxiety Disorders Interview Schedule, and State-Trait Anxiety Inventory for Children (STAI-C). 11 anxiety and 7 CVS subjects had ≥1 anxiety disorder. 82% in the anxiety and CVS groups met criteria for an anxiety disorder on the SCARED. Combining groups, cortisol increased from baseline to recovery during the TSST-C (p=0.0004) and the stressor to recovery (p=0.005). α-amylase did not differ during the TSST-C for the total sample, but increased for anxiety compared to controls from baseline to recovery (p=0.01). HRV decreased during the stressor (p=0.0001) and increased at recovery (p=0.004). No associations were found between biomarkers and trait anxiety. Associations were found between baseline HRV and pre-test state anxiety (r=−0.406, p=0.012) and between recovery HRV and post-test state anxiety (r=−0.501, p=0.002) for the total sample. Anxiety is prevalent in CVS warranting screening. HRV may serve as a biomarker for evaluating stress as a potential trigger for CVS episodes. State but not trait anxiety was associated with changes in HRV, suggesting acute anxiety may be more relevant in linking stress and CVS episodes.

Keywords: Alpha amylase; Child anxiety; Cyclic vomiting syndrome; Heart rate variability; Salivary cortisol; Trier Social Stress Test.

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Cited by 2 articles

Publication types

Research Support, N.I.H., Extramural

Grant support

UL1 TR001082/TR/NCATS NIH HHS/United States

13. Cyclic Vomiting Syndrome in Infants and Children: A Clinical Follow-Up Study


Authors

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PMID: 26861170
DOI: 10.1016/j.pediatrneurol.2016.01.001

Abstract

Background: Cyclic vomiting syndrome is characterized by recurrent vomiting that is associated with increased adrenocorticotropic hormone and antidiuretic hormone levels during cyclic vomiting syndrome attacks. However, both prognosis and treatment remain unclear. We therefore evaluated the clinical features, prognosis, and effectiveness of the prophylaxis of cyclic vomiting syndrome as well as the relationship between symptoms and adrenocorticotropic hormone/antidiuretic hormone levels.

Methods: We included 31 patients with cyclic vomiting syndrome who were admitted to Teikyo University between 1996 and 2008. All patients were diagnosed with cyclic vomiting syndrome based on the criteria of the second edition of the International Headache Classification. The patients (25 of 31) were followed until 2013.

Results: The median overall duration of the disorder was 66 (3-179) months. Follow-up was completed for 25 patients with cyclic vomiting syndrome, of whom 44% (n = 11) developed migraine. Valproic acid, valproic acid with phenobarbital, phenobarbital, and amitriptyline were
effective in nine, four, three, and one patients, respectively. Abnormally high adrenocorticotropic hormone (n = 17) and antidiuretic hormone (n = 18) levels were found among the 25 patients for whom follow-up data were available. The following correlations were significant: attack duration and adrenocorticotropic hormone levels (correlation coefficient: 0.5153, P = 0.0084) and attack duration and antidiuretic hormone levels (correlation coefficient: 0.5666, P = 0.0031). Antidiuretic hormone levels in patients with bilious vomiting were higher than in those without bilious vomiting (P = 0.048).

**Conclusions:** Most patients with cyclic vomiting syndrome recovered completely and benefited from prophylactic therapy, although half of them developed migraines.

**Keywords:** International Headache Classification; adrenocorticotropic hormone; antidiuretic hormone; migraine; prophylactic therapy.

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14. **Challenges With Acute Care and Response to Treatment Among Adult Patients With Cyclic Vomiting Syndrome**


**Author**

Ashley D Jensen ¹

**Affiliation**

- ¹ Ashley D. Jensen, PhD, RN, is Graduate Student, University of Arkansas for Medical Sciences, Little Rock.
- PMID: 26626034
- DOI: 10.1097/SGA.0000000000000148

**Abstract**

Cyclic vomiting syndrome is a chronic gastrointestinal tract disorder. The symptoms include cycles of extreme nausea, vomiting, and abdominal pain separated by periods of wellness. Previous research suggests a quality gap in early recognition and appropriate management of adults with cyclic vomiting syndrome. The purpose of this study was to explore and describe adult patients' experiences with cyclic vomiting syndrome, including challenges receiving a diagnosis and responses to treatment. This study was conducted using a phenomenological research design. A purposeful sample included 16 adult patients with cyclic vomiting syndrome. All data were collected electronically via Survey Monkey and analyzed using content analysis and constant comparison techniques. Two global themes emerged from the data. These were perceived lack of knowledge among healthcare providers and responses to cyclic vomiting syndrome-related treatments. Perceived lack of healthcare provider knowledge contributed to diagnostic delay, inappropriate treatment, and avoidance of care. A combination of medications aimed at managing symptoms and inducing sleep was the most effective abortive medical regimen described. Marijuana use was common. Hot-water bathing was practiced by users and nonusers of marijuana.

- Cited by 2 articles

**Publication types**

- Research Support, Non-U.S. Gov't

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15. **Anxiety Measures Predict Health-Related Quality of Life in Children and Adolescents With Cyclic Vomiting Syndrome**


**Authors**

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PMID: 26095286
DOI: 10.1016/j.jpeds.2015.05.032

Abstract

Objective: To evaluate the relationship between anxiety and health-related quality of life (HRQoL) in children and adolescents with cyclic vomiting syndrome (CVS).

Study design: Forty children aged 8-18 years diagnosed with CVS and 40 parents completed the Screen for Child Anxiety Related Emotional Disorders (SCARED) and the child and parent forms of the Pediatric Quality of Life Generic Core Scale, a measure of HRQoL.

Results: Eleven of the 40 children (27%) by self-report and 6 of 40 (15%) by parent-proxy report met the clinical cutoff for an anxiety disorder on the SCARED. Parent and child SCARED ratings were moderately correlated (intraclass correlation coefficient 0.68; P < .001). Child-rated HRQoL (mean ± SD, 74.3 ± 15.2) and parent-rated HRQoL (mean, 72.1 ± 14.6) were lower than healthy norms (P < .001). Disease severity (mean duration of CVS episodes, 3 ± 2.4 days), annual frequency of CVS episodes (mean, 8.2 ± 15.3), chronicity of CVS (mean, 5.8 ± 3.4 years), and delay in diagnosis (mean, 2.4 ± 1.9 years) were not associated with child-reported HRQoL; however, child SCARED scores accounted for approximately 50% of the variance in child-reported HRQoL (adjusted R² = 0.49; df = 1, 38; P < .001).

Conclusion: Children and adolescents with CVS appear to be at increased risk for anxiety. Anxiety symptoms are a stronger predictor of HRQoL than disease characteristics in children and adolescents with CVS. Assessment and treatment of anxiety in children and adolescents with CVS may have a positive impact on HRQoL.

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Cited by 6 articles

16. Cyclical Vomiting Syndrome: Recognition, Assessment and Management  Free PMC article

Authors
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PMID: 25254185
PMCID: PMC4162439
DOI: 10.5409/wjcp.v3.i3.54

Abstract

Cyclical vomiting syndrome (CVS) is a functional, debilitating disorder of childhood frequently leading to hospitalization. Affected children usually experience a stereotypical pattern of vomiting though it may vary between different individuals. The vomiting is intense often bilious, and accompanied by disabling nausea. Identifiable precipitating factors for CVS include psychosocial stressors, infections, lack of sleep and occasionally even food triggers. Often, it may be difficult to distinguish episodes of CVS from other causes of acute abdomen and altered consciousness. Thus, the diagnosis of CVS remains largely one of exclusion. Investigations routinely done during the work-up of a child with suspected CVS include both blood and imaging modalities. Plasma lactate, ammonia, amino acid and acylcarnitine profiles as well as urine organic acid profile are indicated to exclude inborn errors of metabolism. The treatment remains challenging and targeted at prevention or shortening of the attacks and can be
considered as abortive, supportive and prophylactic. Use of non-pharmacological therapy is also part of the management of CVS. The prognosis of CVS is variable. More insight into the pathogenesis of this disorder as well as role of non-pharmacological therapy is needed.

**Keywords**: Childhood; Cyclical vomiting syndrome; Investigations; Pathogenesis; Treatment.

- Cited by 3 articles
- 1 figure

**Publication types**
- Review

17. **Efficacy of the neurokinin-1 Receptor Antagonist Aprepitant in Children With Cyclical Vomiting Syndrome**


**Authors**
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- PMID: 24898244
- DOI: 10.1111/apt.12822

**Abstract**

**Background**: Aprepitant (Emend, Merck Sharp & Dohme Ltd, Haarlem, the Netherlands), a neurokinin-1 receptor antagonist, prevents vomiting in a range of conditions. No data are available on its use in children with cyclical vomiting syndrome (CVS).

**Aim**: We investigated the efficacy of aprepitant as prophylactic treatment or acute intervention in CVS children refractory to conventional therapies.

**Methods**: Forty-one children (median age: 8 years) fulfilling NASPGHAN criteria treated acutely (RegA) or prophylactically (RegP) with aprepitant were retrospectively reviewed. Primary outcome was the clinical response (decrease in frequency and intensity of CVS episodes). Secondary outcomes were: number of CVS episodes/year, number of hospital admissions/year, CVS episode duration, number of vomits/h, symptom-free interval length (days), and school attendance percentage. The follow-up period was 18-60 months.

**Results**: Sixteen children received RegP and 25 RegA. One child on RegP stopped treatment due to severe migraine. At 12-months on intention-to-treat analysis, 13 children on RegP (81%) achieved either complete (3/16, 19%) or partial (10/16, 62%) clinical response. On RegA, 19 children (76%) had either complete (3/25, 12%) or partial (16/25, 64%) response (P = 0.8 vs. RegP). In both RegP and RegA, there was a significant decrease in CVS episodes/year, hospital admission number/year, CVS episode length, number of vomits/h, as well as an increase in symptom-free interval duration and school attendance percentage. Side effects were reported only in RegP (5/16, 31%) including hiccough (3/16, 19%), asthenia/fatigue (2/16, 12.5%), increased appetite (2/16, 12.5%), mild headache (1/16, 6%) and severe migraine (1/16, 6%).

**Conclusion**: Aprepitant appears effective for both acute and prophylactic management of paediatric cyclical vomiting syndrome refractory to conventional therapies.

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- Cited by 15 articles

**Publication types**
- Clinical Trial

18. **Cyclic Vomiting Syndrome: Treatment Options**


**Authors**
Cyclic vomiting syndrome is a disorder characterized by recurrent episodes of severe nausea and vomiting separated by symptom-free periods. Our aims were to review treatments of adult cyclic vomiting syndrome as well as to identify areas for further clinical research and the unanswered questions in this field. We conducted a PubMed search using such keywords as "cyclic vomiting syndrome," "nausea," "vomiting," "treatment," "trigger factors" and "tricyclic antidepressants" and combined this information with the knowledge and clinical research from the authors. Available data show that in adult cyclic vomiting syndrome, there is an impressive and sustained response to high-dose tricyclic antidepressants. In up to 13% who are regarded as poor responders to tricyclic antidepressants, a predictable profile can be identified related to coexisting psychological disorders, marijuana use, poorly controlled migraine headache or chronic narcotic use. Cyclic vomiting syndrome in adults is being an increasingly recognized entity. Tricyclic antidepressants are the main treatment for controlling symptoms. Eliminating and addressing trigger factors are an essential part of management.

19. Approach to the Diagnosis and Treatment of Cyclic Vomiting Syndrome: A Large Single-Center Experience With 106 Patients

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PMID: 24842256
DOI: 10.1016/j.pediatrneurol.2014.02.009

Abstract
Background: Cyclic vomiting syndrome is characterized by repeated, stereotypical vomiting episodes. The diagnosis is made by exclusion of other organic diseases, which can lead to extensive testing. It has been suggested that these patients can have mitochondrial dysfunction. The aim of the study was to examine the evaluation of our cyclic vomiting patients and to determine whether they had associated, undiagnosed metabolic abnormalities.

Methods: This retrospective study included 106 patients aged <21 years at diagnosis. Information regarding medical history, laboratory, and imaging studies were collected. Metabolic studies in plasma and urine were obtained when patients were well and when patients were in a vomiting cycle, including plasma amino acids, acylcarnitines, and urine organic acids.

Results: The mean age at diagnosis was 8.9 ± 5.0 years. Neuroimaging revealed previously unknown intracranial abnormalities in <10% of patients, none of whom explained the vomiting
signs. Abdominal ultrasounds revealed abnormalities in 15% of patients during an acute episode and 7% of patients when well. Sixty-one patients had an upper gastrointestinal series, all of which were normal. A total of 92% of patients had laboratory testing with 38% indicating abnormalities possibly suggesting mitochondrial dysfunction.

Conclusions: This large, single-center study further evaluated the need for more focused evaluation in patients with suspected cyclic vomiting syndrome. Thirty-eight percent of our patients had abnormalities in blood and/or urine suggesting mitochondrial dysfunction, which requires more detailed investigation in the future.

Keywords: metabolic testing; mitochondrial disorder; pediatrics; vomiting.

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20. From Heave to Leave: Understanding Cyclic Vomiting Syndrome Free PMC article

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PMID: 24304524
PMCID: PMC7309299
DOI: 10.1097/SGA.000000000000013

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.

1 figure

Grant support
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21. Neurochemical Mechanisms and Pharmacologic Strategies in Managing Nausea and Vomiting Related to Cyclic Vomiting Syndrome and Other Gastrointestinal Disorders

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PMID: 24161560
Abstract
Nausea and vomiting are common gastrointestinal complaints which could be triggered by stimuli in both the peripheral and central nervous systems. They may be considered as defense mechanisms when threatening toxins/agents enter the gastrointestinal tract or there is excessive retention of gastrointestinal contents due to obstruction. The pathophysiology of nausea and vomiting is complex and much still remains unknown. Therefore, treatments are restricted or ineffective in many cases. Nausea and vomiting with functional etiologies including cyclic vomiting syndrome are challenging in gastroenterology. In this article, we review potential pathways, neurochemical transmitters, and their receptors which are possibly involved in the pathophysiology of nausea and vomiting including the entity cyclic vomiting syndrome.

Keywords: Cyclic vomiting syndrome; Nausea; Physiopathology; Treatment; Vomiting.
23. **The Management of Cyclic Vomiting Syndrome: A Systematic Review**

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**PMID:** 22634989
**DOI:** 10.1097/MEG.0b013e328355638f

**Abstract**
Cyclic vomiting syndrome (CVS) is a rare abnormality of the neuroendocrine system that affects 2% of children. It is a frequently missed diagnosis in the emergency department and may require a number of emergency department visits before the diagnosis is made. The objectives of this review are to identify the clinical features that suggest a diagnosis of CVS and to review the literature on its management. The MEDLINE and EMBASE databases were searched from January 1948 to October 2011 using the keywords 'Cyclic' or 'Vomiting'. Papers were excluded if they did not follow the consensus guidelines or if they were case reports. This review analysed 1093 cases of cyclic vomiting in 25 papers that fulfilled the inclusion criteria. All except one paper were retrospective studies. The size of these cohort studies ranged from three to 181 patients, with a mean patient size of 29. This review found that over 40% of patients have headaches/migraines, with associated anxiety and depression in ≈ 30% of cases. There is a family history of headaches/migraines in 38.9%, and this association was much stronger in the adult CVS cohort compared with the paediatric cohort. Compared with paediatric CVS, adults have a longer duration of attacks and they occur more frequently (5.9 vs. 3.4 days, 14.4 vs. 9.6 episodes/year). Limited data are available on the treatment of the acute phase of CVS, but in adults, sumatriptan has been shown to be effective. For prophylactic treatment, tricyclics are effective in both adult and paediatric CVS, with a clinical response in 75.5 and 67.6% of patients, respectively, in nonplacebo-controlled cohort studies. Furthermore, propranolol has been shown to be useful in children. CVS is an intractable illness with a major impact on the patient's quality of life. There is a long duration between the onset of symptoms and the diagnosis of the condition. There is a high association with headaches/migraines and anxiety/depression. The symptoms are more severe in adult-onset CVS. Tricyclic antidepressants have good efficacy in reducing the frequency/duration or the intensity of attacks. There is limited evidence on the acute management of CVS.

**Publication types**
- Review
- Systematic Review

24. **High Degree of Efficacy in the Treatment of Cyclic Vomiting Syndrome With Combined Co-Enzyme Q10, L-carnitine and Amitriptyline, a Case Series**
Free PMC article

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- PMID: 21846334
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- DOI: 10.1186/1471-2377-11-102

Abstract

Background: Cyclic vomiting syndrome (CVS), defined by recurrent stereotypical episodes of nausea and vomiting, is a relatively-common disabling and historically difficult-to-treat condition associated with migraine headache and mitochondrial dysfunction. Limited data suggests that the anti-migraine therapies amitriptyline and cyproheptadine, and the mitochondrial-targeted cofactors co-enzyme Q10 and L-carnitine, have efficacy in episode prophylaxis.

Methods: A retrospective chart review of 42 patients seen by one clinician that met established CVS diagnostic criteria revealed 30 cases with available outcome data. Participants were treated on a loose protocol consisting of fasting avoidance, co-enzyme Q10 and L-carnitine, with the addition of amitriptyline (or cyproheptadine in those < 5 years) in refractory cases. Blood level monitoring of the therapeutic agents featured prominently in management.

Results: Vomiting episodes resolved in 23 cases, and improved by > 75% and > 50% in three and one additional case respectively. Among the three treatment failures, two could not tolerate amitriptyline (as was also the case in the child with only > 50% efficacy) and one had multiple congenital gastrointestinal anomalies. Excluding the latter case, substantial efficacy (> 75% response) was 26/29 at the start of treatment, and 26/26 in those able to tolerate the regiment, including high dosages of amitriptyline.

Conclusion: Our data suggest that a protocol consisting of mitochondrial-targeted cofactors (co-enzyme Q10 and L-carnitine) plus amitriptyline (or possibly cyproheptadine in preschoolers) coupled with blood level monitoring is highly effective in the prevention of vomiting episodes.

Cited by 22 articles

12 references

Publication types

- Research Support, Non-U.S. Gov't

25. Psychiatric Co-morbidity and Efficacy of Mirtazapine Treatment in Young Subjects With Chronic or Cyclic Vomiting Syndromes: A Case Series Free PMC article


Authors

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- PMID: 21860824
- PMCID: PMC3155068
- DOI: 10.5056/jnm.2011.17.3.305

Abstract

The aim of this case report was to evaluate the psychiatric co-morbidity and efficacy of mirtazapine treatment in young subjects with chronic or cyclic vomiting syndromes. This is a case series of 8 young subjects (age range of 6-16 years, 11.12 ± 3.52 years) who were referred or consulted to child psychiatry department. They were referred or consulted by pediatric gastroenterology or surgery departments for the presence of non-remitting and medically unexplained vomiting. They were investigated for co-morbid psychiatric disorders using a
structured psychiatric interview. An open trial of mirtazapine was conducted for the treatment and/or prevention of vomiting. Primary outcome measure was Clinical Global Impression-Improvement scale. Subjects were diagnosed with chronic (n = 5) or cyclic (n = 3) vomiting syndromes. Duration of vomiting ranged from 6 months to 10 years (3.5 ± 3.2 years). All subjects received multiple psychiatric diagnoses with anxiety disorders being the most frequent. Maximum mirtazapine dosage was 7.5-30 mg/day (16.00 ± 6.16 mg/day). Three subjects showed complete remission and 5 subjects showed much to very much improvement in vomiting. Most frequent side effects were increased appetite, weight gain and sedation. Young subjects with chronic or cyclic vomiting may frequently suffer anxiety and/or depressive symptoms or disorders. Mirtazapine could be an effective treatment option for the treatment of vomiting and co-morbid anxiety or depressive disorders in these subjects. More systematic research are needed on this topic.

Keywords: Anxiety; Child; Familial cyclic vomiting syndrome; Gastrointestinal diseases; Mirtazapine.

Conflict of interest statement
Conflicts of interest: None.

26. **Sumatriptan as a Treatment for Cyclic Vomiting Syndrome: A Clinical Trial**

**Authors**
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**PMID:** [21147834](https://www.ncbi.nlm.nih.gov/pubmed/21147834)

**DOI:** [10.1177/0333102410390398](https://doi.org/10.1177/0333102410390398)

**Abstract**

**Background and objective:** Cyclic vomiting syndrome (CVS) is associated with migraine. This study aimed to evaluate the efficacy of sumatriptan in treating CVS.

**Methods:** Twelve patients were enrolled in this trial. Sumatriptan was administered either subcutaneously [(age x 4 + 20)/100 x 3 mg] or by nasal spray (NS; 20 mg). Response to the treatment was classified as complete, effective, or noneffective.

**Results:** Eleven patients, who presented with 35 attacks, were treated by subcutaneous injection of sumatriptan. The treatment was responsive in 19 attacks. The efficacy of sumatriptan was high in attacks that occurred in cases with a family history of migraine compared to those without (p = .0482). Five patients were treated with sumatriptan NS for six attacks. The treatment was completely responsive in two of six attacks. We observed no adverse effects associated with sumatriptan treatment in this trial.

**Conclusion:** We conclude that sumatriptan has potential efficacy in treating patients with CVS.

**Cited by 14 articles**

**Publication types**
- Clinical Trial
- Comparative Study

27. **Breaking the Cycle: Cognitive Behavioral Therapy and Biofeedback Training in a Case of Cyclic Vomiting Syndrome**
The present article presents a case of cognitive behavioral therapy (CBT) along with heart rate variability (HRV) biofeedback training for the treatment of a medication unresponsive 13-year-old boy with cyclic vomiting syndrome (CVS). CVS is characterized by recurring stereotypic episodes of vomiting, interspersed with asymptomatic periods. Triggers for vomiting include anticipatory anxiety related to school examinations, family conflicts, and birthday parties as well as infectious diseases, and certain foods. Current treatment design addressed two pivotal etiological factors: autonomic dysregulation and anticipatory anxiety. Treatment outcome suggests that vomiting episodes may be successfully prevented by aiding the patient to identify and manage precipitant psychological stressors, to regulate HRV patterns, and gain a renewed sense of bodily control and self-efficacy. Further research is suggested using a controlled study with pre- and post-behavioral and stress measures to evaluate the effectiveness of CBT and biofeedback training compared to pharmacotherapy and placebo.

28. Cyclical Vomiting Syndrome: Diagnosis, Causes and Treatment
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PMID: 20222244
DOI: 10.7748/ns2010.02.24.23.35.c7550
Abstract
Cyclical vomiting syndrome (CVS) is a disorder of unknown cause. Patients experience episodes of sudden violent vomiting that last from a few hours to a few days, which can occur several times a year. CVS affects children and adults yet despite numerous studies the cause of the condition is unknown. The aim of this article is to outline the current theories for the possible causes of CVS and to examine the various treatment options available.

29. Efficacy of Flunarizine in the Prophylaxis of Cyclical Vomiting Syndrome and Abdominal Migraine
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Abstract
Cyclical vomiting syndrome (CVS), and abdominal migraine (AM) are relatively unusual periodic
syndromes, generally believed to be migraine equivalents, and are characterized by recurrent and severe paroxysmal episodes of vomiting and/or abdominal pain lasting hours to days, separated by weeks to months of no symptoms. Flunarizine is a calcium channel-blocking agent that has been used successfully as a prophylactic agent in the prevention of both childhood and adult-onset migraine syndromes. The purpose of this study was to evaluate the efficacy of flunarizine as a prophylactic/preventive agent in the treatment of CVS and AM. Eight children with CVS and 10 children with AM were included in the study. The mean dose of flunarizine was 5 mg/day in children with CVS, and 7.5 mg/day in children with AM. Follow-up ranged from 6 to 24 months (mean 13 months). There was a 57% reduction in frequency and 44% reduction in duration of attacks of CVS, and a 61% reduction in frequency and 51% reduction in duration of attacks of AM. Sixty-four percent of patients with CVS and AM had history of episodic recurrent headaches with 60% reduction in frequency of attacks on treatment. Flunarizine showed to be equally efficacious than previously tried therapies in the prophylaxis of a small cohort of patients with CVS and AM.

- Cited by 8 articles

30. Cyclical Vomiting Syndrome

Author
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Abstract
Cyclical vomiting syndrome is an uncommon, disabling symptom complex of unknown cause, with features in common with migraine. It affects principally children and adolescents. Differential diagnosis and theories of pathogenesis are discussed. Therapy should be aimed at prophylaxis of vomiting bouts, ‘switching off’ episodes once they commence and preventing complications of established vomiting episodes. Families need rapid access to care to minimize morbidity and disruption to functioning.

Databases searched: CINAHL, Cochrane, Embase, Emcare, Medline, NICE, PsycInfo, Psychological & Scientific Behaviour (Ebsco), PubMed, UpToDate

Search terms: cyclical vomiting syndrome

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