

Treating children's cyclic vomiting

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ABSTRACT

QUESTION One of my pediatric patients was diagnosed with cyclic vomiting syndrome, and the parents are understandably frustrated with the recurrent yet unpredictable episodes that control and disrupt their family life. Are there any effective treatments for this condition?

ANSWER There is currently no evidence-based treatment regimen for cyclic vomiting syndrome. Pharmacologic remedies, according to anecdotal cases, retrospective reports, and open-label trials, have found that some antimigraine, antiemetic, prokinetic, and anticonvulsant agents have been effective. Management focuses on correct diagnosis of the syndrome, avoidance of potential triggers, prophylactic pharmacotherapy, and supportive care for children and their families during episodes.

RÉSUMÉ

QUESTION On a diagnostiqué le syndrome du vomissement cyclique chez un de mes patients pédiatriques et les parents, bien entendu, sont frustrés par les épisodes récurrents mais imprévisibles, qui perturbent leur vie familiale. Existe-t-il des traitements efficaces pour ce problème?

RÉPONSE Il n'existe actuellement aucune thérapie fondée sur des données scientifiques pour le syndrome du vomissement cyclique. Selon des cas cliniques isolés, des rapports rétrospectifs et des études ouvertes, certaines pharmacothérapies, comme les agents antiémétiques, stimulants de la motilité gastrique, anticonvulsifs et contre la migraine, se sont révélées efficaces. La prise en charge se concentre sur le diagnostic exact du syndrome, l'évitement des déclencheurs potentiels, la pharmacothérapie prophylactique, et le soutien aux enfants et à leur famille pendant les épisodes.

Since it was first described in 1882, cyclic vomiting syndrome (CVS) has become an increasingly recognized disorder. It is still poorly understood, however. Current diagnostic criteria established in 1994¹ describe CVS as a pattern of severe episodic vomiting lasting hours or days, separated by symptom-free intervals of varying duration. It affects up to 1.9% of school-aged children.² Besides relentless vomiting, children are usually lethargic (91%) and pale (87%), and have abdominal pain (80%), anorexia (74%), and nausea (72%).³ Even with these established diagnostic criteria, CVS remains a diagnosis of exclusion with unknown etiology, pathophysiology, and target organs.¹

Although CVS is a self-limiting disorder,⁴ its resolution is impossible to predict, and observation without intervention prolongs children's suffering and increases the likelihood of complications, such as dehydration. Cyclic vomiting syndrome is a source of substantial morbidity: 50% of children with CVS require intravenous rehydration. Children with CVS miss a mean of 20 days of school each year.³ The average cost of emergency department visits, hospital stays, diagnostic tests, and missed work is estimated at more than \$17 000 (US) yearly per child with CVS.³

Difficulties with treatment

Initial treatment of CVS is challenging, mainly due to the difficulty of diagnosis. It is an underrecognized disorder that has no laboratory, radiographic, or endoscopic markers.⁴ Differential causes of episodic vomiting that can mimic idiopathic CVS include neurologic (secondary to brainstem neoplasm), endocrine (Addison disease), metabolic (disorders of fatty acid oxidation), and congenital (malrotation or nonfixation of the small intestine) anomalies.⁵ Confusion with acute viral gastroenteritis, food poisoning, gastroesophageal reflux disease, or psychogenic vomiting can lead to surgical fundoplication or hospitalization for psychiatric reasons.³ It is crucial to maintain a high index of suspicion for this disorder and exclude the specific, often treatable, underlying disorders that can be found in 12% of patients.⁵

Pharmacologic interventions

Currently, there are no guidelines for treating CVS. Unknown pathophysiology, no controlled drug trials, and a placebo response as high as 70% lead to only empiric rather than evidence-based therapy.^{3,4} Use of both established and newer antimigraine, antiemetic, and anticonvulsant agents has been successful to some extent, as reported in anecdotal cases, retrospective reports, and open-label trials. It is often necessary to try

several medications until effective treatment with tolerable side effects and no contraindications is found.¹

Avoiding precipitating events is one way of managing CVS. Patients can identify triggers of CVS in 68% of cases; these are often infections (41%) and psychological stress (34%).³ In cases where psychological stress initiates an episode, acute stress management techniques or benzodiazepines can occasionally prevent expected attacks.³ Other predisposing conditions are chronic sinusitis, menstrual periods, motion sickness, and metabolic stress.

Prophylactic therapy with antimigraine agents, prokinetics, and anticonvulsants is recommended when episodes occur more frequently than once a month or when episodes are particularly severe and disabling.^{3,6} The potential correlation between CVS and migraine was postulated in 1904, and recent literature supports this linkage,⁷ laying out the hypothesis that CVS might be an earlier phase of migraine and can progress to migraine headaches.⁸ Children with CVS have a high prevalence of migraines,⁷ frequently have a positive family history of migraines, and have a high response rate to migraine treatments.^{7,9}

It is thus appropriate to start antimigraine prophylaxis, especially in those with a positive family history and those who develop migraine headaches.^{7,9} Among antimigraine agents, amitriptyline is 77% to 91% effective, cyproheptadine (now discontinued) was 40% to 83% effective, and propranolol is 66% to 75% effective at reducing the number of episodes or the severity of episodes (duration of emesis) by 50%.^{7,9} Empiric antimigraine therapy is a cost-effective approach for initial assessment of CVS, but must be accompanied by upper gastrointestinal series with small-bowel follow through to rule out common surgical conditions, such as malrotation or volvulus.^{3,5,6} Erythromycin, a prokinetic agent, acts as a motilin agonist that promotes gastric motility. Its use should be considered if underlying dysmotility is suspected.¹⁰ An open trial of erythromycin in 20 patients 2 to 16 years old with CVS showed that 75% of them had at least a 50% reduction in frequency of vomiting.¹⁰ In an open-label trial, barbiturates, such as phenobarbital, reduced vomiting in 79% of 14 patients 3 to 13 years old.¹¹ Finally, levocarnitine administration was shown to reduce the number of episodes of CVS in 6 patients 1 to 15 years old.¹²

Abortive medications can be used when children break through prophylactic therapy, have prodromal symptoms, or have less frequent episodes.³ Antimigraine agents and antiemetics are usually used. Sumatriptan, a serotonin receptor agonist, is an antimigraine drug that substantially decreases frequency, duration, and intensity of CVS attacks in children.^{7,13} The treatment appeared both safe and cost-effective in an open-label trial and could be delivered subcutaneously.¹³ Other triptans must be taken orally, and therefore, are not as

useful for children who are vomiting. Ondansetron, a serotonin receptor antagonist,³ is a nonsedating, nonanalgesic antiemetic with a high therapeutic index and a 76% efficacy rate in reducing the severity of vomiting by 50%.⁷

Supportive therapy

Once an episode begins, supportive therapy is needed. Vomiting is thought to originate in the brain, not the gastrointestinal tract, so sleep is often the only relief.⁴ A quiet, dark room is a nonstimulating environment that will help patients sleep. Combinations of antiemetics and sedatives, such as the benzodiazepine lorazepam, the sedating antihistamine diphenhydramine, and the antiemetic chlorpromazine, seem to be more effective at treating nausea than antiemetics alone are.³

Management of possible acute complications is also crucial. Intravenous fluids containing 10% dextrose should be given to prevent dehydration and electrolyte imbalance and to terminate ketosis.³ If the acidity of the emesis falls below 4.5, intravenous histamine (H₂) blockers, such as ranitidine or omeprazole, can be given to prevent peptic esophagitis.⁴ Even drinking fluids can offer relief by diluting acid and bile and making emesis less of a contact irritant to the esophagus and mouth.

Finally, family support is an integral part of management. Families need support to deal with the frustration of coping with this unpredictable, disruptive, unexplained illness that is not only typically misdiagnosed but for which there are few definitive answers.⁴ Physicians can provide hope by ruling out serious underlying organic disease, stating that the natural course of CVS ends in recovery in most cases, and offering continuity of care and accessibility until the disorder remits. A definitive diagnostic consultation has been shown to diminish the frequency of episodes even before medications are given.⁴ Parents should also be encouraged to take an active role in reducing the psychological and social effects of CVS.

Conclusion

Cyclic vomiting syndrome remains an elusive disorder for which treatment is mostly empiric. Although some drugs have been shown to be effective in some cases, they do not always work. Advocating for better recognition, proper diagnosis, and further double-blind placebo-controlled trials of therapy would advance our understanding of the mechanisms and treatment of CVS.



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