

# Cyclic vomiting syndrome in children

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## Abstract

**Question** Several children in my office have recurrent vomiting events and they usually end up in the emergency department for intravenous rehydration. One of them has been suffering from those attacks approximately once per month for the past 2 years, leading to a reduction in her quality of life. What is known about cyclic vomiting syndrome and can it be prevented?

**Answer** Cyclic vomiting syndrome includes severe episodic vomiting lasting for hours or days, separated by symptom-free intervals. This gut-brain interaction is poorly understood and is difficult to diagnose. Children suffer from relentless vomiting, lethargy, abdominal pain, anorexia, and nausea. Half of the children require intravenous rehydration. Once diagnosis is made, supportive measures to reduce suffering are recommended and include administering fluids, encouraging sleep, promoting quiet environments, and administering antiemetics or sedatives. In adults, tricyclic antidepressants such as amitriptyline, as well as topiramate as second-line therapy, have been proposed for prophylactic treatment. However, pediatric data are very limited and evidence does not support any recommended course of prophylactic therapy for children with the condition.

Cyclic vomiting syndrome (CVS) includes severe episodic vomiting lasting hours or days, separated by symptom-free intervals of varying duration, and can appear in children and adults. Even though this gut-brain interaction was first described in 1882, the phenomenon is still poorly understood and remains a diagnosis of exclusion with unknown cause, pathophysiology, and target organs.<sup>1</sup>

The definition of CVS is confusing for both providers and patients alike, and some differences exist between the 2008 North American Society for Pediatric Gastroenterology, Hepatology and Nutrition definition<sup>2</sup> and the Rome IV classification.<sup>3</sup> The latter suggests that all of the following conditions must be met to be considered CVS: the occurrence of 2 or more periods of intense, unremitting nausea and paroxysmal vomiting, lasting hours to days within a 6-month period; the episodes are stereotypical in each patient; the episodes are separated by weeks to months, with return to baseline health between episodes; and after appropriate medical evaluation, the symptoms cannot be attributed to another condition.

Cyclic vomiting syndrome affects 1% to 2% of children and recent data suggest a rise in the rate of diagnosis among adults.<sup>4</sup> Among more than 20 000 adults hospitalized for CVS in the United States, 63% were White, 18% were Black, and 6% were Hispanic.<sup>5</sup> Besides having relentless vomiting, children are usually lethargic (91%) and pale (87%), and have abdominal pain (80%), anorexia (74%), and nausea (72%).<sup>6</sup> Cyclic vomiting syndrome is a source of substantial morbidity, with half of children requiring intravenous rehydration.<sup>6</sup> In a recent retrospective study from 3 tertiary academic centres with 57 children, family history of migraine was reported in half (47%) of children, with most children having at least 1 episode every month (63%) and at least 1 known

prodrome (75%).<sup>7</sup> Mean (SD) age of onset of symptoms for children in one study was 5.7 (0.3) years and mean (SD) age of diagnosis was 8.0 (0.3) years.<sup>2</sup>

Misdiagnosis of CVS is frequent, owing to nonspecific presentation and similarity to common conditions such as recurrent gastroenteritis, food poisoning, and eating disorders.<sup>8</sup> The pathophysiology of CVS is not yet known and because of the complexity of the emetic reflex, several theories exist, including autonomic abnormalities, hypothalamic-pituitary-adrenal axis activation, genetic abnormalities, neuronal hyperexcitability, and gastric dysmotility.<sup>9</sup>

## Supportive therapy

Once diagnosis is made, family physicians can recommend supportive measures to reduce suffering among children. Sleep is often the only relief and a quiet, dark room is a nonstimulating environment that can help patients sleep. Frequently, a combination of antiemetics or sedatives, such as diphenhydramine, chlorpromazine, ondansetron, and lorazepam, provides supportive measures during a vomiting episode.

Early recognition of dehydration, at times based on the anticipated course of the episode in view of prior incidents, should prompt use of intravenous fluids and monitoring of electrolyte imbalance and possible ketosis.

Families need support to deal with the frustration of coping with this unpredictable, disruptive, and unexplained illness that is not only typically misdiagnosed but for which there are few definitive answers.<sup>8</sup>

## Prophylactic treatment

While CVS episodes are typically self-limited, the long nature of episodes in some children and increased frequency of episodes in others warrant the use of prophylactic treatment. Current options are described only


for the adult population and include tricyclic antidepressants such as amitriptyline, as well as topiramate as second-line therapy.<sup>10</sup> Adverse events associated with amitriptyline therapy, such as fatigue, weight gain, QT prolongation, and hallucinations, limit topiramate's use.<sup>10</sup>

In a large cohort of adults from Milwaukee, Wis, 65% of patients (88 out of 136) responded to topiramate in an intent-to-treat analysis, with a decreased annual number of CVS episodes (18.1 vs 6.2;  $P < .0001$ ), CVS-related emergency department visits (4.3 vs 1.6;  $P = .0029$ ), and CVS-related hospitalizations (2.0 vs 1.0;  $P = .035$ ).<sup>11</sup> Response to treatment was associated with higher dose, prophylactic use for a year or more, and use of topiramate as monotherapy. However, 55% experienced side effects, resulting in a third of patients discontinuing treatment.<sup>11</sup>

Pediatric data are very limited. In 2011, Boles reported results of implementing a "loose protocol" in which a few children avoided fasting, and received coenzyme Q10 and L-carnitine with the addition of amitriptyline (for those older than 5 years) in refractory cases of CVS.<sup>12</sup> In a retrospective study from Turkey, the efficacy of topiramate compared with propranolol for CVS episode prophylaxis was examined in 16 treatment-naïve children. The study reported that topiramate led to a significant decrease in the number of CVS episodes per year ( $P = .001$ ).<sup>13</sup> Most (81%) children in the topiramate group reported freedom from attacks and 13% had a decrease of more than 50% in attacks per year. Minor adverse effects (drowsiness, nervousness, and dizziness) were observed in a few patients.<sup>13</sup>

In the recent Italian study of 57 children, investigators found no differences in age of onset, gender, duration of follow-up, severity, medication, family history, or trigger factors between children who undertook resolution of vomiting and those who did not, or between children who suffered from migraine and those who did not at follow-up.<sup>7</sup> When discharged from the hospital, 47 of the children (82%) were started on long-term prophylactic treatment with flunarizine, cyproheptadine, topiramate, or proton pump inhibitors.

## Early recognition

Family physicians, with early recognition, evaluation, prompt management during episodes, and referral to further care when intravenous rehydration is needed, can help improve outcomes among children. Understanding the triggers, neuroendocrine mechanism, relationship to migraine, and ways to abort vomiting early in the course of illness will help children cope with CVS. 

### Competing interests

None declared

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