CYCLIC VOMITING SYNDROME

DEPARTMENT OF NEUROLOGY

INTRODUCTION

- Cyclic vomiting syndrome (CVS) is an idiopathic disorder characterized by recurrent, stereotypical bouts of vomiting with intervening periods of normal health. Although it appears to primarily affect children, it is being recognized increasingly in adults.
- Episodes are stereotypical with regard to timing of onset, symptoms, and duration
- A critical fourth criterion that has been added subsequently includes the absence of an organic cause of vomiting

Li, BU, Lefevre, F, Chelimsky, GG, et al. NASPGHAN consensus statement on the diagnosis and management of cyclic vomiting syndrome. J Pediatr Gastroenterol Nutr 2008;.

EPIDEMIOLOGY

- CVS is no longer considered to be rare in children. A cross-sectional study of school-age children in Aberdeen, Scotland, estimated that 34 of 2165 children (1.6 percent) fulfilled the diagnostic criteria for CVS . Their average age was 9.6 years at the time of diagnosis, while the average age at the onset of symptoms was 5.3 years. The overall gender ratio was equal, although, among younger children, it was more common in boys.

(Lucarel - Eur J Pediatr 2000)

PATHOGENESIS

- The pathogenesis of CVS remains unknown, although it may represent a heterogeneous group of disorders.
- CVS and migraines — CVS has been linked to migraine headaches and abdominal migraine This connection is based upon the discreteness of episodes, the progression from cyclic vomiting to migraine headaches in many patients, the presence of a strong family history of migraine headaches in affected children (approximately 80 percent), and the response to antimigraine therapy in up to 80 percent of children

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- Metabolic disorders - MELAS ,about one-half of patients with CVS have evidence for maternal inheritance of a mitochondrial DNA sequence variation .Compared with controls, mothers of patients with cyclic vomiting syndrome were more likely to have a history of migraine, depression, irritable bowel syndrome, and hypothyroidism (Boles- Am J Med Genet A 2005)
- Hypothalamic-pituitary-adrenal axis defects
- Food allergy — Sensitivity to cow's milk, soy, and egg white protein may be related to CVS in children

CLINICAL MANIFESTATIONS

- **Two essential features of CVS**

  * Stereotypical episodes of vomiting regarding onset (acute) and duration (hours to days)

  * The absence of nausea and vomiting between episodes

- **Supportive criteria for the diagnosis of CVS** include a history or family history of migraine headaches, the self-limited nature of the attacks, associated symptoms of nausea, abdominal pain, headache, motion sickness, photophobia, and lethargy, and associated signs of fever, pallor, diarrhea, dehydration, excess salivation, and social withdrawal.

- In children, nausea and possibly lethargy are considered to be key diagnostic features.
- In children, the attacks last an average of 24 to 48 hours. Approximately one-half of children have attacks at regular intervals, commonly occurring every two to four weeks, while the others have an unpredictable temporal pattern of vomiting.
- Approximately two-thirds of parents can identify a trigger, which is usually infectious (upper respiratory) or psychological (negative or positive)

NATURAL HISTORY

- Many children outgrow CVS by their preteen or early teenage years. A minority of children who progress from CVS to migraine headaches will first pass through a phase of abdominal migraines. One retrospective study of 51 children followed for up to 13 years found that vomiting resolved in 60 percent. However, 42 percent continued to have regular headaches and 37 percent had abdominal pain; these features were present even in patients whose vomiting had resolved

  (Fitzpatrick, and al - Outcome for children with CVS- Arch Dis Child 2007)

DIAGNOSIS

NASPGHAN suggests the following diagnostic criteria (all of which must be met) (apply to children and adolescents)

- At least five attacks in any interval, or a minimum of three attacks during a six-month period
- Episodic attacks of intense nausea and vomiting lasting 1 hour to 10 days and occurring at least one week apart
- Stereotypical pattern and symptoms in the individual patient
- Vomiting during attacks occurs at least four times per hour for at least one hour
- Return to baseline health between episodes
- Not attributed to another disorder

TREATMENT

- Patients may require supportive care during severe bouts of cyclic vomiting, which may include admission to a hospital, intravenous fluids, antiemetics, and occasionally analgesics. Children should be referred to a pediatric gastroenterologist, neurologist, or metabolic specialist
- Treatment can also be considered as abortive, prophylactic, and supportive.
- Most treatments have been based upon observational data or clinical experience, forming the basis for the following suggested approach (Grade 2C).

- No specific therapy has been proven to be effective for CVS in controlled trials. However, several empiric treatments have been effective in case series. Treatment with medications should be guided by three considerations :
- Whether there is a family history of migraines
- Frequency of episodes
- Severity of episodes

- A trial of antimigraine medications is reasonable in patients with ± a family history of migraine headaches.
- The decision to administer abortive and/or prophylactic antimigraine medications depends upon the frequency and severity of the attacks.
- Prophylactic daily therapy :if attacks occur more than once every one to two months or are severe enough to require hospitalization or substantial disability.
- Abortive therapy can be used if episodes occur less than once every one to two months or are mild.

- Agents that have been used empirically (with variable success) in children include sumatriptan, propranolol, cyproheptadine, and tricyclic antidepressants
- amitriptyline for prophylaxis in children ≥5ys even if there is no history of headache or a family history of migraine . begin at 0.25-0.5 mg/kg/day orally at bedtime, increase every 1-4 weeks as needed and tolerated by 5-10 mg, until 1-1.5 mg/kg/day (maximum 75 mg per 24 hours). (For dose >1 mg/kg/day, divide twice daily). It typically takes one to three months for the effects of amitriptyline to become evident.

- Use of amitriptyline may be limited in infants and toddlers < 5 years of age due to side effects (such as personality changes, anticholinergic effects, and tachyarrhythmias). The EKG (particularly the QTc interval) and electrolytes (K+, Mag+) should be monitored. Cyproheptadine and propranolol are often used as alternatives. Cyproheptadine is recommended as first-line treatment in children under age 5 years.
- Cyproheptadine 0.25-0.5 mg/kg/day orally divided twice daily or three times daily (maximum 12 mg per 24 hours).

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- **During vomiting episodes**, the goal is to abort or shorten the episode.
- Anecdotal experience in children suggests that intravenous administration of a dextrose 10% solution can decrease the frequency and duration of vomiting episodes in about one-half of patients. In addition to 10 percent intravenous dextrose, anecdotal experience suggests that high dose ondansetron(5HT3 antagonist) (0.3 to 0.4 mg/kg/dose, maximum about 20 mg/dose), sedation and a quiet, dark room are often helpful.

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- **Lifestyle changes**

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- **Avoidance of triggers**
- Avoid fasting (frequent low fat feedings)
- Recognize the potential role of excitement as a trigger (eg, downplay big events)
- Maintain good sleep hygiene (eg, avoid sleep deprivation)
- Avoid triggering foods: chocolate, cheese, monosodium glutamate, antigenic foods
- Avoid excessive energy output

- **Supplemental carbohydrate: for fasting-induced episodes**

  Provide fruit juices, other sugar-containing drinks

  Provide extra snacks between meals, before exertion, or at bedtime

- **Migraine headache lifestyle interventions**

  Regular aerobic exercise (avoid overexercising)

  Regular meal schedules (ie, avoid skipping meals)

  Moderation in consuming or avoidance of caffeine