orphanaesthesia

# Anaesthesia recommendations for patients suffering from

# Cyclical (or cyclic) vomiting syndrome

**Disease name:** Cyclical (or cyclic) vomiting syndrome

**ICD 10:** G43.A0

**Synonyms:** Cyclical vomiting, not intractable; persistent vomiting, cyclical; cyclic vomiting, psychogenic

Cyclical vomiting syndrome (CVS) is a rare condition affecting ~3 in 100,000 children, with Caucasian but no sex predominance. It is generally a disorder of childhood with symptom onset in pre or early school age. Adult cases (onset in 3rd to 4th decade) are also reported. As patients are well in between episodes, there is usually a delay in diagnosis (2-3 years in children, longer in adults), with frequent emergency department presentations. It is a diagnosis of exclusion. Diagnostic criteria have been published by various bodies including the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition, the Rome Foundation (Rome IV 2016 under functional gastrointestinal disorders) and also the International Classification of Headache Disorders (3rd edition beta version). This reflects the uncertainty about the pathophysiology of the syndrome, described variously as functional, psychiatric, neurological either epileptogenic or autonomic dysfunction, association with or triggered by cannabis use versus a migraine variant or as episodic symptoms associated with migraine.

Medicine in progress

Perhaps new knowledge

Every patient is unique

Perhaps the diagnostic is wrong

**Find more information on the disease, its centres of reference and patient organisations on Orphanet: www.orpha.net**

## Disease summary

The pattern experienced by an individual is stereotypical: a prodrome including nausea, a hyperemesis/vomiting phase (typically 6-8 episodes per hour for a few days; associated with continuing nausea, headache and abdominal pain), recovery phase and an asymptomatic phase of a few to several weeks. Episodes are triggered by illness-infection, stress-anxiety, certain foods (similar to migraine triggers), sleep deprivation or physical exhaustion, exposure to cold/heat, allergies, motion sickness or menstruation. The episodes are intractable in nature, significantly impairing quality of life, with associated psychiatric comorbidity of anxiety and depression in a minority (27%).

Mortality is not reported. The prognosis in children is good with a significant percentage (61%) remitting fully in adolescence; although the adolescent may then develop headache and migraine (41%), abdominal pain or irritable bowel syndrome (62%). A genetic component is debated (although none identified) with frequent association of family history of migraine (28%). There are case reports of patients labelled as having this syndrome but the symptoms reflect manifestations of a rarer mitochondrial or metabolic disorder (e.g. porphyria or of fatty acid oxidation such as acylcoenzyme A dehydrogenase deficiencies).

General considerations in approaching patients with CVS (as per the approach for migraine sufferers) is to avoid the individual patient's triggers and other known precipitators, with attention to prophylactic and abortive therapies, supportive care for the patient during episodes and family support. The main anaesthetic concern is management of pre or postoperative pain, nausea and vomiting (and associated patient and family distress if poorly controlled), and consequent dehydration, electrolyte or acid-base derangement and hypoglycaemia, if an episode is precipitated perioperatively. The evidence for abortive or prophylactic intervention is from mostly retrospective case series or case studies. The anaesthetist may be consulted in the non-operative setting by their gastroenterologist or emergency department colleagues for their antiemetic, sedative-anxiolytic expertise (as employed for resistant postoperative nausea and vomiting (PONV)).

## Typical surgery

Patients with CVS will typically present in the pre-diagnosis phase for investigation to rule out underlying organic or mechanical causes of vomiting. Investigative procedures include upper (and lower) gastrointestinal endoscopy (electively or emergently for haematemesis) and imaging (X-ray, ultrasound including Doppler and assessment of bowel wall oedema/thickness [indicating ischemia or resolved obstruction], HIDA scan, CT scan [if MRI unavailable and emergent imaging required] of abdomen with contrast, MRI/MRA of brain or abdomen) to demonstrate gastric emptying and bowel transit, gall bladder or renal pathology, intestinal obstruction (intussusception, malrotation, stricture or web), abdominal arterial or intracranial pathology (such as cerebral/posterior fossa tumour or arterio-venous anomaly/thrombosis). The investigations may be done electively or emergently if symptoms persist beyond 72 hours. Surgical biopsy for samples to rule out mitochondrial/metabolic disease may be requested. For young children, a general anaesthetic is commonly required.

Where the diagnosis is not established, the patients may receive surgery such as laparotomy, laparoscopy and appendicectomy (as abdominal pain is a feature of the syndrome). Other incidental surgery e.g. orthopaedic may be required when the diagnosis is known.

A series of adult patients with refractory CVS have had permanent gastric mucosal stimulators inserted but the level of evidence supporting this practice is low.

## Type of anaesthesia

Although not specifically documented, patients with CVS may be at risk of pre and postoperative nausea and vomiting (PONV). Notably motion sickness, as an identified risk factor for PONV, is prevalent amongst CVS patients (28%). Similar to patients with migraine, avoidance of the patient's known triggers and control of pain, inflammation (particularly when involving the head and neck) and anxiety is desirable. As physical and psychological stress are precipitants of the episodes, the injury or illness prior to and subsequent surgery may trigger prolonged nausea and vomiting, resistant to standard antiemetic therapy. Wherever possible and appropriate, use of local and regional techniques to reduce or avoid general anaesthesia is ideal, along with use of multimodal anaesthesia to reduce or avoid intraoperative and postoperative opioid and or tramadol.

When a patient presents for surgery, a perioperative plan using their usual effective medications (often these are used and are beneficial in acute migraine and migraine prophylaxis) and additional sedative and anxiolytic agents (including benzodiazepines and drugs from the antiepileptic, alpha-2 agonist, antihistamines, and antipsychotic classes) and liberal oral hydration (ideally with balanced rehydration solutions) and/or intravenous fluid supplementation (including glucose 10%) should be instituted. Therapy should be up-titrated to reduce preoperative anxiety (which may precipitate an episode) and commenced the day or night prior (for elective/semi-elective surgery) and a premedication given on the day of surgery (for elective and emergency surgery) with avoidance of prolonged fasting if no intravenous access in situ. Steroids have been used as both abortive and prophylactic therapy. At least three antiemetic interventions (ideally including dexamethasone), as recommended in the 2014 consensus guidelines for PONV should be employed intraoperatively. If GA is required, use of propofol bolus and infusion at sedative levels or as total intravenous anaesthesia (TIVA) is a consideration.

## Necessary additional diagnostic procedures (preoperative)

If the patient has been vomiting preoperatively, assessment of hydration, electrolyte, acid-base and glucose status and renal function, with correction of derangement is advisable. Hypo- or hyper-natraemia is possible depending on the amount of water intake and salt supplementation tolerated. Acidosis and elevated lactate can occur in the setting of profound dehydration. Hypoglycaemia may occur with prolonged fasting and vomiting.

## Particular preparation for airway management

Nil specific: rapid sequence induction is a consideration depending on the surgical indication, if an emergency procedure and if vomiting preoperatively. Gastric emptying is reported as usually normal or rapid in children and most adults with CVS, with a subset of adults with reduced transit (opioid or marijuana users and diabetic patients).

## Particular preparation for transfusion or administration of blood products

Nil reported.

## Particular preparation for anticoagulation

Nil reported.

## Particular precautions for positioning, transport or mobilisation

Nil reported. Patients may experience motion sickness. Transport in the left lateral position with suction available and the option to position the bed/transport trolley in trendelenberg is appropriate in anticipation of vomiting with movement and on emergence from anaesthesia.

## Probable interaction between anaesthetic agents and patient's long term medication

Patients with CVS may be on prophylactic therapy (not supported by randomised trials to date) such as propranolol, clonidine, antiepileptics (sodium valproate, topiramate, gabapentin, lamotrigine, and cabamazepine*),* tricyclic antidepressants (amitriptyline or nortriptyline 1-2 mg/kg), barbituates, antihistamines (including cyproheptadine), calcium channel blockers (e.g. flunarizine), mitochondrial therapy such as L-carnitine, co-enzyme Q10 or riboflavin and pizotifen (the latter like propranolol used in abdominal migraine) and previously erythromicin. They may also take opioids or present to emergency departments for systemic opioids for pain management. Marijuana (illicit and prescribed dronabinol) use is reported as alleviating symptoms by patients but can also be the causative agent (cannabinoid hyperemesis syndrome). Opioid and marijuana use and tolerance are relevant to the patient's perioperative anaesthetic and analgesic requirements. If arteriovenous thrombosis is suspected the patients may be on antiplatelet therapy which has both surgical and anaesthesia import if regional analgesia being considered. Multimodal analgesia with non-opioid analgesia and use of opioid-sparing agents is desirable e.g paracetamol and non-steroidal anti-inflammatory drugs. Prophylactic therapy for CVS can be opioid sparing and thus escalated in the perioperative setting to optimise analgesia. Patients with CVS will usually have plans for abortive (for use in the prodrome) and or rescue therapy including 5HT-3 antagonists, other antiemetics, sumatriptan, benzodiazepines, barbituates, antihistamines and proton pump inhibitors or H2 antagonists.

Usual care should be taken with particular attention to the co-administration of medications which may cause hypotension and bradycardia, sedation (which may be desirable), prolongation of the QT interval or serotonergic syndrome such as tramadol. As the latter can cause nausea and vomiting to the same extent as opioids, it may also be best avoided.

If the patient has been experiencing nausea or vomiting and received an antiemetic agent preoperatively, then an agent from a different class should be administered for intraoperative antiemetic therapy and postoperatively. Prescription of more than one agent using a tiered approach in the postoperative phase is desirable (as recommended for PONV). Consider antipsychotic/sedative medications earlier in the CVS patient's PONV algorithm.

## Anaesthesiologic procedure

Avoid patient's usual triggers.

Nil specifc anaesthetic literature beyond 1 adult anaesthetic case report and 4 paediatric patients (1 case report and 1 case series) admitted with resistant CVS requiring anaesthetist intervention.

Consideration of sedative-anxiolytic premedication.

Avoid prolonged fasting and dehydration preoperatively and encourage preprocedure fluid intake of balanced oral rehydration solution (if not experiencing an episode). Preoperative glucose and electrolyte monitoring and supplemental intravenous hydration (including glucose supplementation) and correction of electrolyte-acid base derangement as indicated.

Rapid sequence induction of GA when clinically indicated (active vomiting or emergency procedure).

Recommendations are as for patients with high risk of PONV.

Intravenous induction where possible with propofol by standard induction bolus 1-3 mg/kg and during maintenance either infusion at subhypnotic doses e.g.120 mcg/kg/h or as total intravenous anaesthesia (TIVA). Minimum triple antiemetic intervention (including dexamethasone particularly, as steroids have been used as abortive therapy) intraoperatively. Consideration of sedative-anxiolytic supplementation prior to emergence depending on dose and agent used preoperatively e.g. benzodiazepine, alpha-2 adrenergic agonist.

Use of multimodal non-opioid/opioid-sparing analgesia including paracetamol, nonsteroidal anti-inflammatory drugs, local and regional anaesthesia where possible.

Attention to intra and postoperative electrolytes, glucose and intravenous fluid management aiming for positive fluid balance.

## Particular or additional monitoring

Regular assessment of fluid balance, hydration, electrolyte, glucose and renal status if vomiting. Renal impairment can have implications for drug accumulation/toxicity and dosing.

## Possible complications

Triggering of a vomiting episode with consequent dehydration and derangement of electrolyte, acid-base balance, glucose and renal function.

Control of postoperative pain and inflammatory response, where possible, to avoid adjunctive triggers is important.

## Postoperative care

Usual care with attention to hydration, electrolyte, glucose and renal status if vomiting. Prescription of postoperative fluids including glucose supplementation, with availability of multiple antiemetics and sedatives-anxiolytics, specifying an escalation plan in the event of nausea or frequent vomiting, including acid suppression therapy. As for a patient admitted with migraine, consider nursing the patient in a quiet single room that can be darkened. For nausea and vomiting resistant to intermittent medications, continuous infusions that could be instituted include clonidine (0.15-0.3 mcg/kg/h), dexmedetomidine (0.25-0.5mcg/kg then 0.25 mcg/kg/h), midazolam (0.02 mg/kg/h) and a subhypnotic dose of propofol (as above). Depending on the institution's local practice, the patient may require admission to high dependency care for these infusions and monitoring of their fluid balance.

## Information about emergency-like situations / Differential diagnostics

The stress of an emergency and or the event of surgery may trigger an episode. The nausea and vomiting of an episode may be indistinguishable from PONV as a complication of anaesthesia and surgery initially, and may then transform into the stereotypical vomiting frequency for the patient.

Differential diagnoses include vertigo, pregnancy (hyperemesis gravidarum), ureteropelvic junction obstruction, nephrolithiasis, migraine (particularly basilar), adrenocortical insufficiency, metabolic genetic disorders such as acute intermittent porphyria, hyperammonaemia or fatty acid oxidation defect (such as an acylcoenzyme A dehydrogenase deficiency). If the CVS is persistent, or associated with resistant hypoglycaemia (especially if non-ketotic), then specialist metabolic consultation is warranted to direct testing such as for acetylcarnitine and urine organic acid assays (at a time of stress) and gene testing (if indicated). Diabetes mellitus and gastroparesis may be associated with CVS.

## Ambulatory anaesthesia

Nil reported. Attention to antiemetic interventions as per non-ambulatory anaesthesia.

## Obstetrical anaesthesia

Nil reported.

## Literature and internet links


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**Links**

http://www.romecriteria.org/assets/pdf/19_RomeIII_apA_885-898.pdf

http://www.ihs-classification.org/_downloads/mixed/International-Headache-Classification-III-ICHD-III-2013-Beta.pdf

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