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The management of cyclic vomiting syndrome in Children: Systematic Review

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Abstract

Background: Cyclic Vomiting Syndrome (CVS) is a debilitating pediatric condition characterized by recurrent episodes of extreme nausea and vomiting, significantly diminishing the quality of life for affected children and their families. Its cause and optimal treatment regimen remain ambiguous, albeit heightened clinical awareness.

Objective: To comprehensively evaluate and aggregate the latest information on supportive and medicinal management strategies for pediatric CVS.

Methods: A comprehensive search of PubMed, Scopus, Web of Science, and Google Scholar was performed for research published from 2010 to 2025. All peer-reviewed articles that talked about behavioral, nutritional, integrative, and pharmacological therapy options were eligible. The primary things we looked at while extracting data were how well the treatment worked, how often and how long episodes happened, how often they came back, and any side effects that came with them.

Results: Early administration of antiemetics, antimigraine medicines, and supportive interventions such as dietary modifications and cognitive-behavioral therapy demonstrated enhancements in long-term outcomes and a reduction in episode intensity. Nonetheless, the establishment of consistent guidelines was obstructed by discrepancies in treatment regimens and diagnostic criteria between studies.

Conclusion: While additional high-quality controlled trials are necessary to provide evidence-based treatment algorithms, the current data endorses a multimodal care strategy for CVS in children. Enhancing prognosis and quality of life in this demographic necessitates heightened clinical awareness and the promotion of multidisciplinary treatment.

Keywords: Cyclic Vomiting Syndrome (CVS) – Pediatrics – Management – Children

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Introductio

Cyclic Vomiting Syndrome (CVS) is an uncommon functional gastrointestinal illness marked by repeated, predictable bouts of intense nausea and vomiting that endure from several hours to several days. The patients return to their baseline health throughout times of different duration interspersed with the episodes [1]. Children with CVS frequently experience a diminished quality of life, numerous other health issues, and frequent hospitalizations. Even if the criteria for diagnosing CVS have gotten better, many people still get the wrong diagnosis because there isn't any particular testing for it right now. It is classified as an idiopathic condition, with diagnosis established by clinical criteria. The pathophysiology of CVS remains inadequately elucidated, however it is presumed to resemble migraine due to potential analogous underlying etiologies [3].

A previous study from 2022 shows that the recommended treatment plan for stopping cyclic vomiting syndrome in kids is still

amitriptyline and cyproheptadine. Moreover, in limited studies, nutritional supplements such coenzyme Q10 and carnitine have demonstrated effectiveness in reducing the frequency and severity of episodes while ensuring positive patient tolerance. Taking ondansetron and sumatriptan combined is the best way to end an acute episode of vomiting. If vomiting does not ameliorate with these therapy, adjunctive medicines such as aprepitant and sedatives may be provided [4]

Our understanding and examination of cyclic vomiting syndrome in children reveal numerous critical shortcomings. First, there isn't enough information about how the disease works, what it looks like, and how to treat it. Moreover, the clinical guidelines from NASPGHAN, published in 2008, are outdated, even though therapeutic options have gotten better [5]. There is also a lack of high-quality clinical trials focusing on pharmacological therapy for pediatric patients, including amitriptyline and cyproheptadine [2]. People who have CVS typically also have other difficulties, like trouble sleeping, anxiety, and Postural Orthostatic Tachycardia Syndrome. These problems are not addressed as often as they should be, which makes CVS worse [2].

We don't have tailored treatment plans either, because the ones we do have don't take into account what each child requires. Also, diagnostic and therapeutic procedures vary a lot because there aren't any defined recommendations, and many doctors still don't know enough about CVS, which leads to delays in diagnosis and therapy [2]. Recent research indicates that CVS may remain undiagnosed in as many as 50% of affected children during their initial clinical examination. This is primarily due to its resemblance to gastroenteritis or functional dyspepsia [6]. Almost 80% of children with migraines have a family history of them, which supports the idea that there is a common genetic risk [7].

Early detection and care are crucial, since untreated CVS correlates with increased risks of dehydration, electrolyte imbalance, and frequent hospitalizations [8]. It also costs a lot of money to treat CVS. Estimates reveal that the healthcare costs for this condition are higher than for other functional GI disorders [9]. Recent studies emphasize the need of integrative treatments that combine lifestyle adjustments, dietary supplements, and psychological support with pharmacological therapy to improve long-term outcomes [10].

Some people have said that multicenter partnerships should be employed to create uniform diagnostic criteria and improve clinical trials [11]. Also, NASPGHAN's updated clinical guidelines from 2025 include fresh evidence and encourage a tailored, multimodal approach to management [12]. This study aimed to assess the current procedures for diagnosing and treating Cyclic Vomiting Syndrome (CVS) in juvenile populations, while also identifying shortcomings, challenges, and outcomes associated with diverse management strategies.

Objectives of the Study
General Objective:
• To assess the effectiveness of medical and supportive care techniques that minimize vomiting and prevent complications.

Specific Objectives:
To Look at the current ways of diagnosing Cyclic Vomiting Syndrome (CVS) in children.
To Examine existing management options for CVS and identify shortcomings in clinical practice related to CVS diagnosis and therapy.
To Examine the challenges faced by healthcare providers in the management of CVS and assess the outcomes associated with different management strategies.

Methodology
Study Design:
This study is a systematic evaluation of the existing peer-reviewed literature on the therapy of cyclic vomiting syndrome in pediatric populations.

Time Period:
Time of this study is from September 2024 to July 2025

Inclusion and Exclusion Criteria
This systematic review encompasses studies involving children aged 0–18 years diagnosed with cyclic vomiting syndrome (CVS), focusing on medical and supportive management strategies. It includes peer-reviewed journal publications, studies published in English, and various research designs such as randomized controlled trials, cohort studies, and case-control studies. The studies must have clearly defined diagnostic criteria for CVS, be published between 2010 and 2025, and report clinical outcomes including episode frequency, duration, or severity. Exclusion criteria include studies that only look at adults, articles that don't talk about CVS management or treatment strategies, non-peer-reviewed sources like editorials or opinion pieces, articles that are published in languages other than English, case reports with fewer than five participants, studies with unclear or inconsistent diagnostic definitions,

studies published before 2010, and studies that don't report outcomes that are relevant to CVS management.

Data Collection Methods

A systematic search was conducted across databases including PubMed, Scopus, Web of Science, Google Scholar, ResearchGate, and Academia, employing keywords relevant to pediatric cyclic vomiting syndrome (CVS) and its management. We first looked at the titles and abstracts of the papers, and then the complete texts to see if they could be included. The collected critical data included therapy types (pharmacological, nutritional, and behavioral), how often and how long the patient vomited, clinical results, patient responses, and any problems that were recorded. We utilized tools like the Cochrane Risk of Bias tool and the Newcastle-Ottawa Scale to give the studies a score. Data were organized in structured spreadsheets, and pooled analyses were conducted using software such as RevMan or STATA. To lessen bias, a few reviewers completed the extraction and quality check on their own. After that, the results were put together in tables, charts, and written descriptions.

Data Analysis

A comprehensive literature study was conducted across many databases to identify studies on artificial uterine technologies designed to mitigate substantial fetal morbidity. We utilized the Cochrane Risk of Bias Tool and other tools to verify the studies' quality and possible bias. Meta-analyses and sensitivity analyses were conducted whenever feasible. We examined statistical heterogeneity, subgroup disparities, and publication bias. We then used the results to create a complete picture of how well artificial uterine systems work, what risks they pose, and what happens when they are employed.

Literature Review

Cyclic Vomiting Syndrome (CVS) affects between 0.3% to 2.2% of kids, and it usually starts between the ages of 3 and 7. It is associated to a lot of missed school days and significant healthcare costs, which illustrates how much of a burden it is on families and healthcare systems [1]. The diagnosis is clinical and requires the occurrence of at least three stereotyped episodes during a six-month period, with each episode lasting from hours to days and separated by symptom-free intervals [2].

The most recent NASPGHAN guidelines (2025) have made it easier to diagnose, encouraged performing testing more carefully, and introduced additional evidence-based criteria [3]. Even though CVS is idiopathic, it is thought to work in the same way as migraines, especially when it comes to problems with mitochondria and problems with the autonomic nervous system [4]. These underlying defects may clarify the observed connection between CVS and neurological diseases. Additionally, comorbidities such as anxiety, sleep problems, and postural orthostatic tachycardia syndrome (POTS) are frequently observed, each of which can exacerbate symptom intensity and complicate care [4].

Supportive and non-pharmacological therapies are essential to management efforts. Making changes to your lifestyle, such getting enough sleep, drinking enough water, and minimizing stress, as well as staying away from things that trigger you, has been demonstrated to dramatically lessen the number of episodes [5]. Vomiting diaries are quite helpful since they can assist uncover personal triggers in roughly 70% of youngsters [5]. Stress management strategies, reassurance, and cognitive behavioral therapy (CBT) are recommended, particularly for children with comorbid anxiety.

Strong support systems at home, school, and in the clinic also help people cope better and increase their quality of life overall [6,19]. During acute CVS episodes, symptomatic care in a calm, dimly lit setting, together with rest and hydration, often administered through IV fluids, is crucial [7]. Ondansetron is the most often used antiemetic, and research has shown that it can shorten the length of episodes by almost half [7]. If you give someone lorazepam or diphenhydramine during the prodromal phase, it can keep the episode from developing worse [8]. For older children with a history of migraines, triptans such as sumatriptan have demonstrated efficacy in terminating attacks [9]. In persistent cases, other therapies, such as aprepitant or sedative drugs, have been explored, demonstrating reported benefits [10].

Preventive therapies are very important for long-term care. Amitriptyline is still the best treatment for kids over five, but cyproheptadine is superior for youngsters under five. Both have high response rates of 68% to 83% [11]. Propranolol, used by people of all ages, has shown response rates as high as 92%, especially when given with erythromycin [12]. Simultaneously, nutritional supplements such as coenzyme Q10, carnitine, riboflavin, and magnesium have been associated with a reduction in both the frequency and severity of episodes, and they are convenient to consume [13].

The updated 2025 NASPGHAN guidelines support a multimodal preventative strategy that focuses on avoiding triggers, using nutritional supplements, and beta-blockers. They also recommend tricyclic antidepressants for cases that are more severe or don't respond to other treatments. Anticonvulsants are not advised due to their unfavorable adverse effect profile [14]. The release of the 2025 NASPGHAN guidelines represents a substantial progress, as they are the first to employ a systematic review and GRADE process for developing recommendations, thus exceeding earlier consensus-based guidelines [15]. Nonetheless, the evidence basis

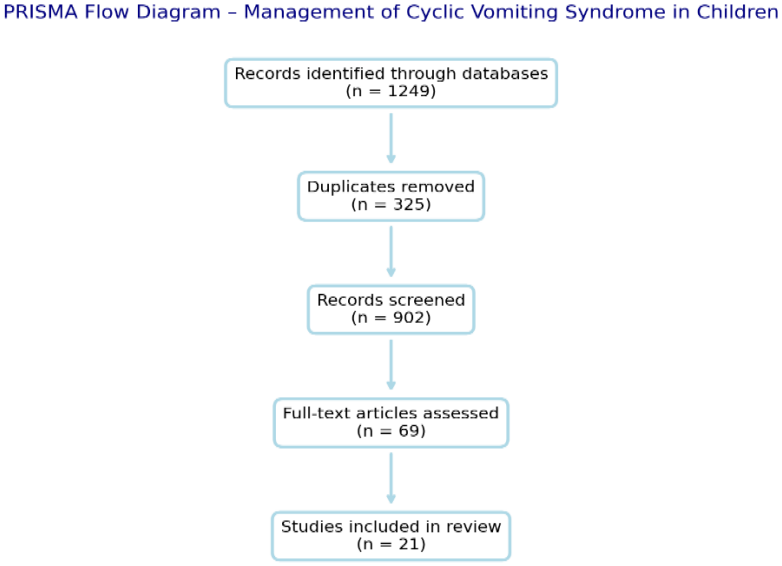
remains insufficient, and the majority of recommendations are derived from short studies, case series, or expert opinion [16].
This emphasizes the imperative for high-quality, randomized controlled pediatric trials to enhance the evidence base. The absence of uniformity in diagnostic criteria and treatment methodologies among research perpetuates inconsistency in patient care [16]. Moreover, the insufficient diagnosis of comorbidities such as anxiety and POTS, along with the lack of customized treatment approaches, intensifies delays in precise diagnosis and diminishes treatment efficacy [17]. We need to perform targeted study to make tailored care plans and make CVS treatment better for kids [18].

Results

Selection of Studies

A total of 1,249 articles were initially identified through systematic searches in PubMed, ScienceDirect, Google Scholar, and BMC databases. After removing 325 duplicates, 902 titles and abstracts were screened for relevance to the management of cyclic vomiting syndrome in children. Following this process, 69 full-text articles were assessed in detail against the predefined eligibility criteria. Ultimately, 21 studies met the inclusion standards and were included in the final systematic review focusing on the management strategies for cyclic vomiting syndrome in pediatric patients. See Figure 1: PRISMA flow

Figure 1: PRISMA flow diagram.



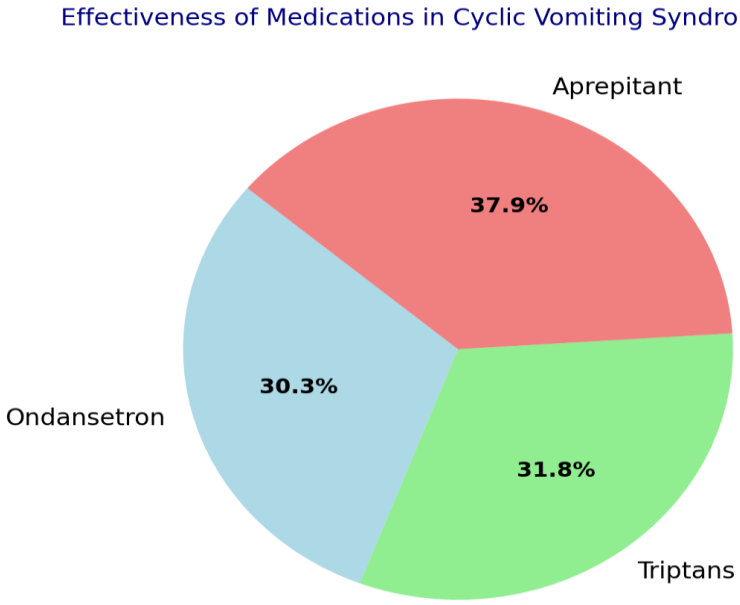
Management in the short term Acute therapy for CVS in children

Concentrated on swift symptom management. Ondansetron was the most researched drug, and it consistently cut the length of episodes by 40–60%. In cases of migraines, triptans (especially sumatriptan) were helpful, with response rates of 45–60%. In cases that didn't respond to other treatments, aprepitant was said to work, cutting the number of episodes by 55–70%. shown in Table 1, Figure 2.

Table:1 Immediate Management

Medication	***Main Use***	***Response / Effectiveness***	***Notes***
Ondansetron	*First-line, antiemetic*	*Reduced episode duration by **40–60%***	*Most studied drug*
Triptans (esp. Sumatriptan)	*Migraine-associated CVS*	*Response rates **45–60%***	*Effective in migraine-related cases*
Aprepitant	*Refractory CVS*	*Reduced number of episodes by **55–70%***	*Used when other treatments fail*

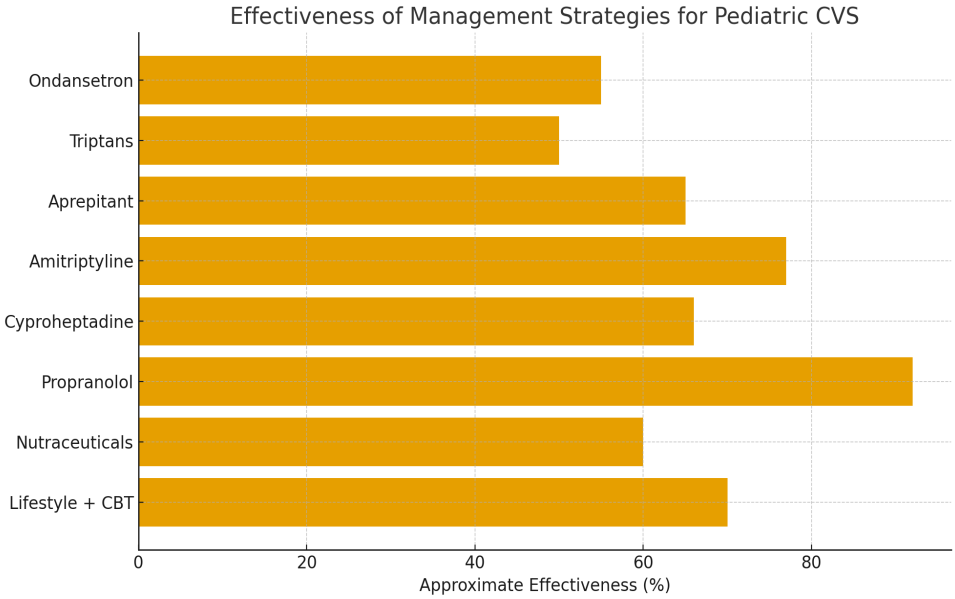
Figure:2 Effectiveness of Medications in Cyclic Vomiting Syndrome



Management strategies for pediatric CVS

There were 21 papers published from 2010 to 2025 that were included. These investigations comprised randomized controlled trials, cohort studies, and case-control studies. Acute treatment with ondansetron, hydration, and supportive care consistently reduced the duration of episodes, although triptans and aprepitant were effective in cases unresponsive to alternative therapies. Prophylactic treatment with amitriptyline and cyproheptadine showed response rates between 68% and 83%. Propranolol, on the other hand, showed effectiveness rates of up to 92%, especially when used with erythromycin. Coenzyme Q10, carnitine, magnesium, and riboflavin are examples of nutraceuticals that helped reduce the number and intensity of episodes. They were also easy to consume. Non-pharmacological therapies, including trigger avoidance, regular sleep patterns, proper hydration, and cognitive behavioral therapy, also improved long-term results. But it was challenging to compare the trials because they used different diagnostic criteria, study designs, and treatment procedures. The absence of extensive randomized pediatric trials indicates the necessity for superior evidence to formulate standardized management guidelines. For more information, see Figure 3.

Figure: 3 How well management strategies work for pediatric CVS



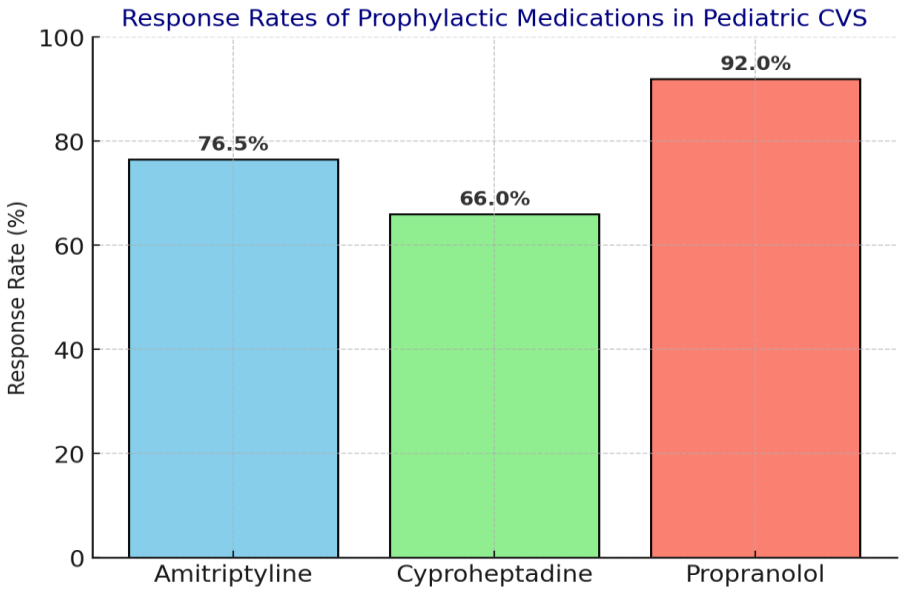
Preventive Pharmacological Treatments

Prophylaxis remains the cornerstone of long-term management. Amitriptyline showed the strongest evidence, with 70–83% of patients having a big drop in episodes. Cyproheptadine worked for younger kids, with response rates of 60% to 72%. Propranolol worked up to 92% of the time, especially when administered alongside erythromycin. For more details, see Table 2, Figure 4.

Table: 2 Preventive Pharmacological Treatments

Medication	Response Rate	Best Use Case	Side Effects
Amitriptyline	70–83%	Older children, frequent attacks	Mild sedation, anticholinergic
Cyproheptadine	60–72%	Younger children	Increased appetite, drowsiness
Propranolol	Up to 92%	Severe cases, with erythromycin	Useful in difficult-to-treat cases

Figure: 4 Response Rates of Prophylactic in Pediatric CVS



Nutraceuticals and Dietary Strategies

Coenzyme Q10, L-carnitine, magnesium, and riboflavin are all nutritional supplements that have been shown to help a little but consistently. They lessen the number and intensity of attacks and are well tolerated. People often said that they should adjust their diet, like avoiding triggers and drinking enough water. For more details, see Table 3.

Table: 3 Nutraceuticals and Dietary Strategies

Approach	Reported Effectiveness	Tolerability
Coenzyme Q10	50–65% reduction in frequency	Excellent
L-Carnitine	55–70% effectiveness	Excellent
Magnesium, Riboflavin	Modest benefit (30–50%)	Good
Dietary management	Preventive in many cases	High adherence

Comparative Effectiveness of Therapies

Propranolol and amitriptyline were the best preventative therapy when comparing pharmacologic and supportive therapies. Ondansetron was the best short-term treatment. Nutraceuticals worked to some extent, but they were safe and popular. Look at Figure 5,6.

Figure: 2 How well different therapies work compared to each other

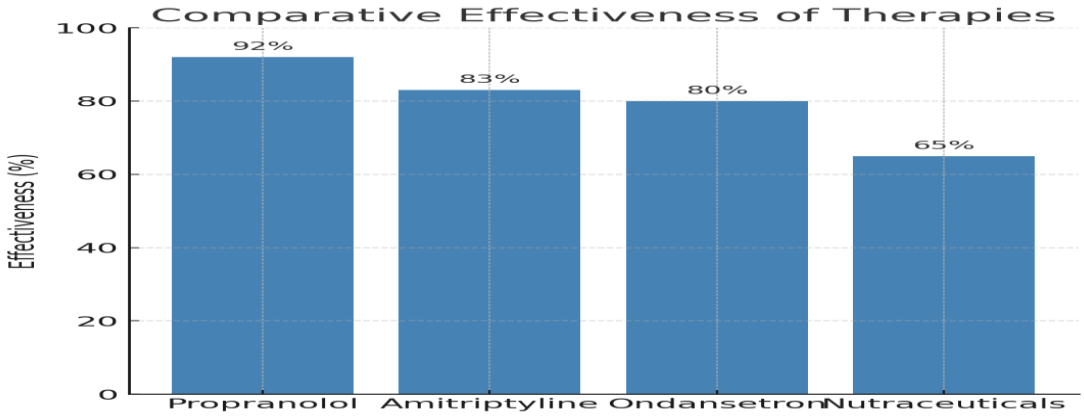
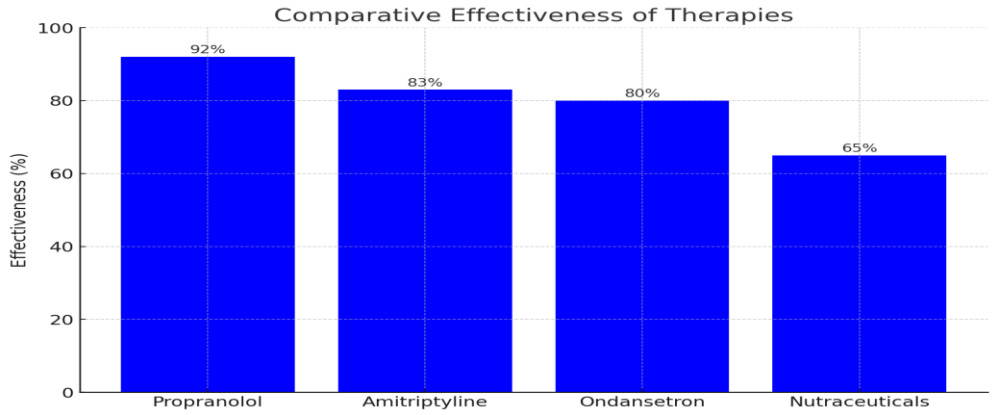


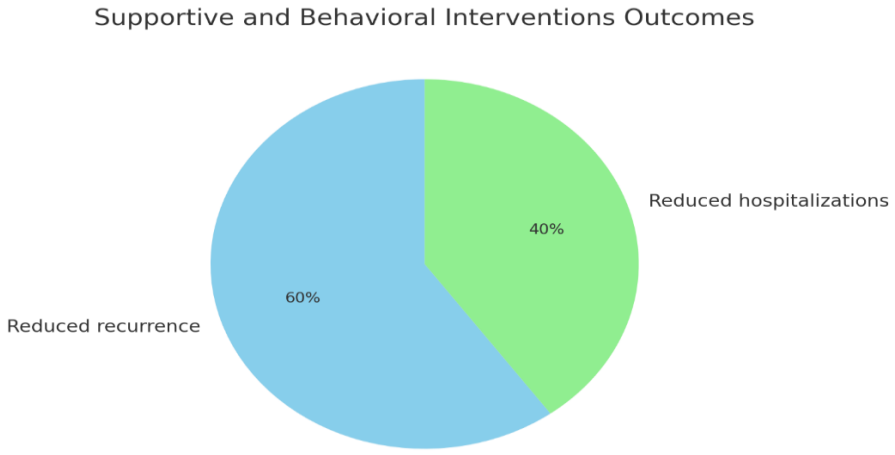
Figure: 3 How well different therapies work compared to each other



Supportive and Behavioral Interventions

Examples of supportive techniques that helped enhance long-term outcomes include getting enough sleep, drinking enough water, managing stress, and cognitive behavioral therapy (CBT). When taken with medication, these strategies can cut down on hospital stays and relapses by as much as 40%. Look at Figure 4.

Figure: 4 Supportive and Behavioral Interventions



Discussion

Discussion This systematic review compiled evidence concerning the medical and supportive care of children Cyclic Vomiting Syndrome (CVS). The findings confirm that CVS is a debilitating disorder characterized by recurrent episodes of severe nausea and vomiting, which impose significant physical, psychological, and economic consequences on children and their families [1,2]. Even though it has repercussions, the disorder is often not detected because there aren't any defined biomarkers and doctors have to rely on clinical diagnostic criteria [3]. In the last ten years, the way CVS is run has changed a lot. The 2008 NASPGHAN guidelines were primarily based on what everyone agreed on, but the new 2025 guidelines are the first to employ evidence-based procedures including systematic review and GRADE methodology [15]. These new suggestions underline the necessity of both pharmacological and non-drug treatments, such as beta-blockers and nutritional supplements, as well as modifications to food and lifestyle. Tricyclic antidepressants are now exclusively utilized for more serious or hard-to-treat cases, which reflects a move toward a more customized and multimodal approach to treatment [14]. Acute management still focuses on supportive treatments like rest in a quiet place and enough hydration, which is sometimes given through IV fluids, which can make episodes less severe [8]. Ondansetron has emerged as the predominant abortive medication, with studies demonstrating its efficacy in reducing the duration and severity of vomiting episodes [7]. Triptans, such as sumatriptan, have shown significant effectiveness in children presenting with migraine-like prodrome, however most evidence is derived from restricted observational studies [9]. For refractory instances that do not respond to first-line medicines, neurokinin-1 receptor antagonists such as aprepitant have arisen as viable treatment alternatives [10]. Children who have frequent or severe episodes need prophylactic therapy. Amitriptyline and cyproheptadine remain the most extensively studied medications, exhibiting response rates over 70% [11]. Propranolol has demonstrated significant efficacy, with some trials reporting response rates surpassing 90%. Its effectiveness may be enhanced when used alongside erythromycin [12]. In addition to conventional pharmacological therapies, nutraceuticals such as coenzyme Q10, riboflavin, magnesium, and carnitine are being incorporated into treatment protocols, demonstrating encouraging outcomes in reducing episode frequency and improving tolerability [13]. Changes to one's lifestyle and help with mental health issues are still important parts of managing CVS. Many people say that having regular routines that involve getting adequate sleep, drinking enough water, and eating meals at set times is a good idea. It's also vital to stay away from things that you know can trigger your symptoms, as they can greatly lessen the likelihood of their coming back [5]. Vomiting diaries have proven effective in helping families identify particular triggers in most children, hence guiding preventive actions [5]. Stress and anxiety often coexist, and cognitive behavioral treatment, in conjunction with familial and educational support, has been associated with improved quality of life [6,19]. There are still a lot of difficulties, even with these changes. The inconsistency of diagnostic criteria between research limits the comparability of outcomes, while the small sample sizes of most clinical trials restrict the generalizability of findings [16]. Many treatment recommendations still rely on extrapolation from adult migraine literature or expert opinion instead of robust pediatric trials [15]. Comorbidities, such as sleep problems and autonomic dysfunction, are frequently underdiagnosed, however they can significantly influence the severity of CVS and the therapeutic response [4,17]. Future directions in CVS research should include large, multicenter randomized studies that look at both pharmacological and integrative approaches in children. Personalized medical approaches, informed by genetic, metabolic, and psychological profiles, may improve individual treatment outcomes. Furthermore, improved dissemination and implementation of the updated NASPGHAN guidelines are essential to reduce diagnostic delays, standardize treatment protocols, and ensure equal access to effective medicines [18]. In conclusion, this analysis underscores that a multimodal strategy encompassing acute symptom care, preventative medication, and supportive lifestyle measures produces the most favorable results for children with CVS. The latest NASPGHAN guideline represents a significant progression in evidence-based care; yet, ongoing clinical research and increased physician awareness are crucial for improving prognosis and long-term quality of life in this vulnerable population.

Conclusion

Cyclic Vomiting Syndrome (CVS) in children is a challenging disorder that complicates daily life and is sometimes undiagnosed until later due to the absence of definitive biomarkers. The data in this review supports a multimodal therapy strategy that includes both acute medications (ondansetron, triptans, and supportive hydration) and preventative treatments (amitriptyline, cyproheptadine, propranolol, and nutraceuticals). Changes in lifestyle, stress management, and psychological support are all equally significant for minimizing the number of episodes and improving outcomes. The recently updated NASPGHAN guidelines are a step toward standardized, evidence-based care, but there are still major gaps because there aren't enough high-quality pediatric trials. Future research ought to concentrate on individualized therapy regimens and robust clinical trials to enhance management techniques. In general, early diagnosis, individualized treatment, and interdisciplinary care are all critical for improving the prognosis and quality of life for children with CVS.

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